TOXICOLOGICAL PROFILE FOR 1,1,2-TRICHLOROETHANE

Agency for Toxic Substances and Disease Registry
U.S. Public Health Service

In collaboration with:
U.S. Environmental Protection Agency

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FOREWORD

The Superfund Amendments and Reauthorization Act of 1986 (Public Law 99-499) extended and amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law (also known as SARA) directed the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare toxicological profiles for hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List and which pose the most significant potential threat to human health, as determined by ATSDR and the Environmental Protection Agency (EPA). The lists of the most significant hazardous substances were published in the Federal Register on April 17, 1987, and on October 20, 1988.

Section 110 (3) of SARA directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list. Each profile must include the following content:

> (A) An examination, summary and interpretation of available toxicological information and epidemiological evaluations on the hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects,
>
> (B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, or chronic health effects, and
>
> (C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

This toxicological profile is prepared in accordance with guidelines developed by ATSDR and EPA. The original guidelines were published in the Federal Register on April 17, 1987. Each profile will be revised and republished as necessary, but no less often than every 3 years, as required by SARA.

The ATSDR toxicological profile is intended to characterize succinctly the toxicological and health effects information for the hazardous substance being described. Each profile identifies and reviews the key literature that

describes a hazardous substance's toxicological properties. Other literature is presented but described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

Each toxicological profile begins with a public health statement, which describes in nontechnical language a substance's relevant toxicological properties. Following the statement is material that presents levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Data needs that are of significance to protection of public health will be identified by ATSDR, the National Toxicology Program of the Public Health Service, and EPA. The focus of the profiles is on health and toxicological information; therefore, we have included this information in the front of the document.

The principal audiences for the toxicological profiles are health professionals at the federal, state, and local levels, interested private sector organizations and groups, and members of the public. We plan to revise these documents as additional data become available.

This profile reflects our assessment of all relevant toxicological testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, EPA, the Centers for Disease Control, and the National Toxicology Program. It has also been reviewed by a panel of nongovernment peer reviewers and was made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.

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Agency for Toxic Substances and
Disease Registry

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1. PUBLIC HEALTH STATEMENT

1.1 WHAT IS 1,1,2-TRICHLOROETHANE

1,1,2-Trichloroethane is a colorless, sweet-smelling liquid that does not burn easily and boils at a higher temperature than water. It is made by two companies in the United States. It is used mostly where l,l-dichloroethene (vinylidene chloride) is made. 1,1,2-Trichloroethane is used as a solvent. Because information about how much is made and how it is used is not available, we cannot say how much 1,1,2-trichloroethane is used, where it is used, or in what products it is found. 1,1,2-Trichloroethane may also be formed in landfills when 1,1,2,2-tetrachloroethane is broken down. When it is released into the environment, most 1,1,2-trichloroethane finally ends up in the air, but some may enter groundwater. Breakdown in both the air and groundwater is slow. In the air, half the 1,1,2-trichloroethane is expected to breakdown in 49 days and so it is likely to spread far from where it is released before breaking down. A few studies show that 1,1,2-trichloroethane below the soil surface or in groundwater does not breakdown within 16 weeks, and other studies suggest that it will last for years. Some studies show that breakdown of 1,1,2- trichloroethane occurs in landfills, but how fast this happens is not known. For more information, see Chapters 3, 4, and 5.

1.2 HOW MIGHT I BE EXPOSED TO 1,1,2-TRICHLOROETHANE?

Low levels of 1,1,2-trichloroethane may be found in outdoor air. The main source of this 1,1,2-trichloroethane is thought to be industries that use it as a solvent. Because the industries that produce 1,1,2-trichloroethane or use it to make other chemicals often recycle or burn their waste, releases of 1,1,2-trichloroethane by these industries should not be major sources of pollution. From surveys of industrial wastewater, we learn that some of the industries that discharge 1,1,2-trichloroethane are the timber products industry, plastics and synthetics industry, and laundries. Limited data show that 1,1,2-trichloroethane is present in a quarter to a half of city air samples. Where 1,1,2-trichloroethane is found, the samples tested usually contain 10 to 50 parts of 1,1,2-trichloroethane per trillion parts of air (ppt). Though exposure to contaminated drinking water taken from groundwater sources is possible, such exposure appears to be rare. A nationwide survey did not find 1,1,2-trichloroethane in drinking water, but well water in some areas has been found to contain it. Surveys found 1,1,2-trichloroethane in well water in Wisconsin, New Jersey, Rhode Island, and Suffolk County, New York. The largest amount in these supplies was 31 parts of 1,1,2-trichloroethane per one billion parts of water (ppb). 1,1,2-Trichloroethane has not been reported in food or soil. Besides the air and drinking water sources, people may be exposed to 1,1,2-trichloroethane from spills and in the workplace, where it may be used as a solvent. Exposure would most likely be from breathing vapors of the chemical or from skin contact. When a chemical like 1,1,2-trichloroethane is utilized to make other chemicals, it

is usually used in tightly closed automatic systems, so that workers are not usually exposed to high levels of it. A national survey conducted in 1981-1983 estimated that 1,036 workers were exposed to 1,1,2-trichloroethane. 1,1,2-Trichloroethane has been found thus far at 45 of 1177 hazardous waste sites on the National Priorities List (NPL) in the United States. Landfill gases from these sites may contain 1,1,2-trichloroethane. For more information, please see Chapter 5.

1.3 HOW CAN l,l,2-TRICHLOROETHANE ENTER AND LEAVE MY BODY?

1,1,2-Trichloroethane can enter the body when a person breathes air containing 1,1,2-trichloroethane, or when a person drinks water containing this compound. It can also enter the body through the skin. After it enters the body, it is carried by the blood to organs and tissues such as the liver, kidney, brain, heart, spleen, and fat. Experiments in which animals were given 1,1,2-trichloroethane by mouth have shown that most 1,1,2-trichloroethane leaves the body unchanged in the breath and as other substances that it was changed into in the urine in about 1 day. Very little stays in the body more than 2 days. More information on how 1,1,2-trichloroethane can enter and leave the body can be found in Chapter 2.

1.4 HOW CAN 1,1,2-TRICHLOROETHANE AFFECT MY HEALTH?

1,1,2-Trichloroethane can cause temporary stinging and burning pain on the skin when humans touch it. There is no other information on the health effects of 1,1,2-trichloroethane in humans. Most of what we know about the health effects of this chemical comes from experiments in animals. As is true with most chemicals, a large amount of 1,1,2-trichloroethane produces more damage than a small amount. Short-term exposure to high levels of 1,1,2-trichloroethane in air or high doses given by mouth or applied to the skin has caused death in animals. Long-term exposure of animals to high doses given by mouth has also shortened the lifespan. These levels and doses are much higher than would be found in the air, water, or food to which humans might be exposed. Breathing high levels in air can affect the nervous system and cause sleepiness. 1,1,2-Trichloroethane may also affect the liver, kidney, and digestive tract, produce skin irritation, and affect the body's ability to fight infections. Mice, but not rats, that were given high doses of 1,1,2-trichloroethane by mouth for most of their life developed liver cancer, but we do not know whether humans exposed to this chemical would develop cancer. From the limited information available in animals, it appears that 1,1,2-trichloroethane does not cause birth defects or otherwise inhibit normal development. More information on the health effects of 1,1,2-trichloroethane can be found in Chapter 2.

1.5 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO 1,1,2-TRICHLOROETHANE?

Although chemists have ways of measuring some chemicals in body fluids,

there is no commonly used medical test to find out whether a person has been exposed to 1,1,2-trichloroethane.

1.6 WHAT LEVELS OF EXPOSURE HAVE RESULTED IN HARMFUL HEALTH EFFECTS?

Tables l-l, l-2, l-3, and l-4 show the link between exposure to 1,1,2-trichloroethane and known health effects. Tables 1-l and l-3 show that no information is available on human health effects from breathing, eating, or drinking 1,1,2-trichloroethane. Minimal Risk Levels (MRLs) are included in Table l-3. These MRLs were derived from animal data for both short- and long-term exposure, as described in Chapter 2 and in Table 2-2. The MRLs provide a basis for comparison to levels which people might encounter either in the air or in food or drinking water. If a person is exposed to 1,1,2-trichloroethane at an amount below the MRL, it is not expected that harmful (noncancer) health effects will occur. Since these levels are based on information that is currently available, there is always some uncertainty associated with it. Also since the method for deriving MRLs does not use any information about cancer, an MRL does not imply anything about the presence, absence, or level of risk of cancer. In Table l-2, death is reported to occur at levels that are less than or equal to the levels that cause central nervous system depression and mild liver effects. However, the period of exposure that produces death is longer. More information on levels of exposure linked with harmful effects can be found in Chapter 2.

1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

The Environmental Protection Agency (EPA) has allowed a limit of 0.6 μg/L (ppb) 1,1,2-trichloroethane in waters such as lakes and streams. The EPA also requires industry to report discharges or spills of 100 or more Pounds.

Levels of 1,1,2-trichloroethane allowed in the workplace are regulated by the Occupational Safety and Health Administration (OSHA). The occupational exposure limit is 10 parts of 1,1,2-trichloroethane per one million parts of air (ppm) for an 8-hour workday, 40-hour workweek. More information on government recommendations can be found in Chapter 7.

1.8 WHERE CAN I GET MORE INFORMATION?

If you have more questions or concerns, please contact your state health or environmental department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road, E-29
Atlanta, Georgia 30333

1. PUBLIC HEALTH STATEMENT

TABLE 1-1. Human Health Effects from Breathing 1,1,2-Trichloroethane*

Short-term Exposure (less than or equal to 14 days)		
Levels in Air (ppm)	Length of Exposure	Description of Effects
		The health effects resulting from short-term human exposure to air containing specific levels of 1,1,2-trichloroethane are not known.
Long-term Exposure (greater than 14 days)		
Levels in Air (ppm)	Length of Exposure	Description of Effects
		The health effects resulting from long-term human exposure to air containing specific levels of 1,1,2-trichloroethane are not known.

*See Section 1.2 for a discussion of exposures encountered in daily life.

TABLE 1-2. Animal Health Effects from Breathing 1,1,2-Trichloroethane

Short-term Exposure (less than or equal to 14 days)		
Levels in Air (ppm)	Length of Exposure	Description of Effects*
416	6 hr	Death in mice.
418	4 hr	Central nervous system depression in mice.
500	8 hr	Death in rats.
800	3 hr	Liver effects in mice.
Long-term Exposure (greater than 14 days)		
Levels in Air (ppm)	Length of Exposure	Description of Effects
		The health effects resulting from long-term animal exposure to air containing specific levels of 1,1,2-trichloroethane are not known.

*These effects are listed at the lowest level at which they were first observed. They may also be seen at the higher levels.

TABLE 1-3. Human Health Effects from Eating or Drinking 1,1,2-Trichloroethane*

Short-term Exposure (less than or equal to 14 days)		
Levels in Food (ppm)	Length of Exposure	Description of Effects
		The health effects resulting from short-term human exposure to air containing specific levels of 1,1,2-trichloroethane are not known.
Levels in Water (ppm)		
10.5		Minimal risk level (derived from animal data; see Section 1.6 for discussion).
Long-term Exposure (greater than 14 days)		
Levels in Food (ppm)	Length of Exposure	Description of Effects
		The health effects resulting from long-term human exposure to food containing specific levels of 1,1,2-trichloroethane are not known.
Levels in Water (ppm)		
1.4		Minimal risk level (derived from animal data; see Section 1.6 for discussion).

*See Section 1.2 for a discussion of exposures encountered in daily life.

TABLE 1-4. Animal Health Effects from Eating or Drinking 1,1,2-Trichloroethane

Short-term Exposure (less than or equal to 14 days)		
Levels in Food (ppm)	Length of Exposure	Description of Effects*
1200	1 day	Liver effects in rats.
Levels in Water (ppm)		
525	1 day	Taste aversion in mice.
670	1 day	Motor impairment in mice
1990	1 day	Death in mice.
5980	1 day	Death in rats.
Long-term Exposure (greater than 14 days)		
Levels in Food (ppm)	Length of Exposure	Description of Effects*
1500	78 weeks	Shortened lifespan in mice.
Levels in Water (ppm)		
200	90 days	Immune system effects in mice.
200	90 days	Liver effects in mice.

*These effects are listed at the lowest level at which they were first observed. They may also be seen at higher levels.

2. HEALTH EFFECTS

2.1 INTRODUCTION

This chapter contains descriptions and evaluations of studies and interpretation of data on the health effects associated with exposure to 1,1,2-trichloroethane. Its purpose is to present levels of significant exposure for 1,1,2-trichloroethane based on toxicological studies, epidemiological investigations, and environmental exposure data. This information is presented to provide public health officials, physicians, toxicologists, and other interested individuals and groups with (1) an overall perspective of the toxicology of 1,1,2-trichloroethane and (2) a depiction of significant exposure levels associated with various adverse health effects.

2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

To help public health professionals address the needs of persons living or working near hazardous waste sites, the data in this section are organized first by route of exposure -- inhalation, oral and dermal -- and then by health effect -- death, systemic, immunological, neurological, developmental, reproductive, genotoxic, and carcinogenic effects. These data are discussed in terms of three exposure periods -- acute, intermediate, and chronic.

Levels of significant exposure for each exposure route and duration (for which data exist) are presented in tables and illustrated in figures. The points in the figures showing no-observed-adverse-effect levels (NOAELS) or lowest-observed-adverse-effect levels (LOAELs) reflect the actual doses (levels of exposure) used in the studies. LOAELs have been classified into "less serious" or "serious" effects. These distinctions are intended to help the users of the document identify the levels of exposure at which adverse health effects start to appear, determine whether or not the intensity of the effects varies with dose and/or duration, and place into perspective the possible significance of these effects to human health.

The significance of the exposure levels shown on the tables and graphs may differ depending on the user's perspective. For example, physicians concerned with the interpretation of clinical findings in exposed persons or with the identification of persons with the potential to develop such disease may be interested in levels of exposure associated with "serious" effects. Public health officials and project managers concerned with response actions at Superfund sites may want information on levels of exposure associated with more subtle effects in humans or animals (LOAEL) or exposure levels below which no adverse effects (NOAEL) have been observed. Estimates of levels posing minimal risk to humans (minimal risk levels, MRLs) are of interest to health professionals and citizens alike.

For certain chemicals, levels of exposure associated with carcinogenic effects may be indicated in the figures. These levels reflect the actual doses associated with the tumor incidences reported in the studies cited. Because cancer effects could occur at lower exposure levels, the figures also show estimated excess risks, ranging from a risk of one in 10,000 to one in l0,000,000 (10^{-4} to 10^{-7}), as developed by EPA.

Estimates of exposure posing minimal risk to humans (MRLs) have been made, where data were believed reliable, for the most sensitive noncancer endpoint for each exposure duration. MRLs include adjustments to reflect human variability and, where appropriate, the uncertainty of extrapolating from laboratory animal data to humans. Although methods have been established to derive these levels (Barnes et al. 1987; EPA 1980c), uncertainties are associated with the techniques.

2.2.1 Inhalation Exposure

Much of the data on the health effects of 1,1,2-trichloroethane following inhalation exposure were taken from a limited, unpublished study conducted by Dow Chemical Company. The original study was not available for review, but a brief description of the results was reported by Torkelson and Rowe (1981). This study is discussed below because in some cases, comparable information was not available from other reports, and in other cases, the levels of exposure associated with effects were noticeably different from those reported in other studies. These data indicate that the health effects of 1,1,2-trichloroethane might occur over a broader range of exposure levels than data from other studies would suggest. Although these results are discussed below, they are not included in Table 2-1 or plotted in Figure 2-1 as levels of significant exposure because the details of experimental methods and results were not provided.

2.2.1.1 Death

No studies were located regarding death in humans following inhalation exposure to 1,1,2-trichloroethane.

Mortality produced by inhalation of 1,1,2-trichloroethane has been studied in animals. Three of 5 rats exposed to 2080 ppm of 1,1,2-trichloroethane for 2 hours died within about 24 hours, but 5 rats exposed to 890 ppm for 2 hours survived (Carlson 1973). Carpenter et al. (1949) exposed rats to 1,1,2-trichloroethane vapor for 4 hours. They reported that 2-4/6 rats died within 14 days following exposure to 2000 ppm and 0-1/6 died following exposure to 1000 ppm. The exact number of rats killed in each treatment group was not reported. Because it was not explicitly stated that no rats died following exposure to 1000 ppm, this concentration was not used as a NOAEL. The LC_{50} of 1,1,2-trichloroethane in rats exposed for 6 hours was 1654 ppm (Bonnet et al. 1980). During exposure, animals are first excited and then somnolent. Most mortality occurred within 24 hours of exposure, but some deaths were reported up to 8 days later. No macroscopic

TABLE 2-1. Levels of Significant Exposure to 1,1,2-Trichloroethane - Inhalation

Graph Key	Species	Exposure Frequency/ Duration	Effect	NOAEL[b] (ppm)	LOAEL[a] (Effect)		Reference
					Less Serious (ppm)	Serious (ppm)	
ACUTE EXPOSURE							
Lethality							
1, 2	rat	2 h		890		2080 (3/5 dead)	Carlson 1973
3	rat	4 h				2000 (2-4/6 dead)	Carpenter et al. 1949
4	rat	6 h				1654 (LC_{50})	Bonnet et al. 1980
5	rat	8 h				999 (LC_{50})	Pozzani et al. 1959
6	rat	8 h				500 (4/6 dead)	Smyth et al. 1969
7	mouse	2 h				12,934 (death)	Lazarew 1929
8	mouse	6 h				416 (LC_{50})	Gradiski et al. 1978
9	mouse	15 h				3750 (death)	Gehring 1968
Systemic							
10, 11	rat	2 h	Hepatic	890	2080 (incr SGPT)		Carlson 1973
12	mouse	3 h	Hepatic		800 (incr SGPT)		Takahara 1986a
13	mouse	15 h	Hepatic		3750 (incr SGPT)		Gehring 1968
Neurological							
14	rat	6 h				1654 (somnolent)	Bonnet et al. 1980
15, 16	mouse	2 h			1833 (lie down on side)	2749 (loss of reflex control)	Lazarew 1929
17	mouse	4 h				418 (CNS depression)	De Ceaurriz et al. 1981
18	mouse	15 h				3750 (anesthesia)	Gehring 1968

[a]LOAEL - Lowest Observed Adverse Effect Level
[b]NOAEL - No Observed Adverse Effect Level

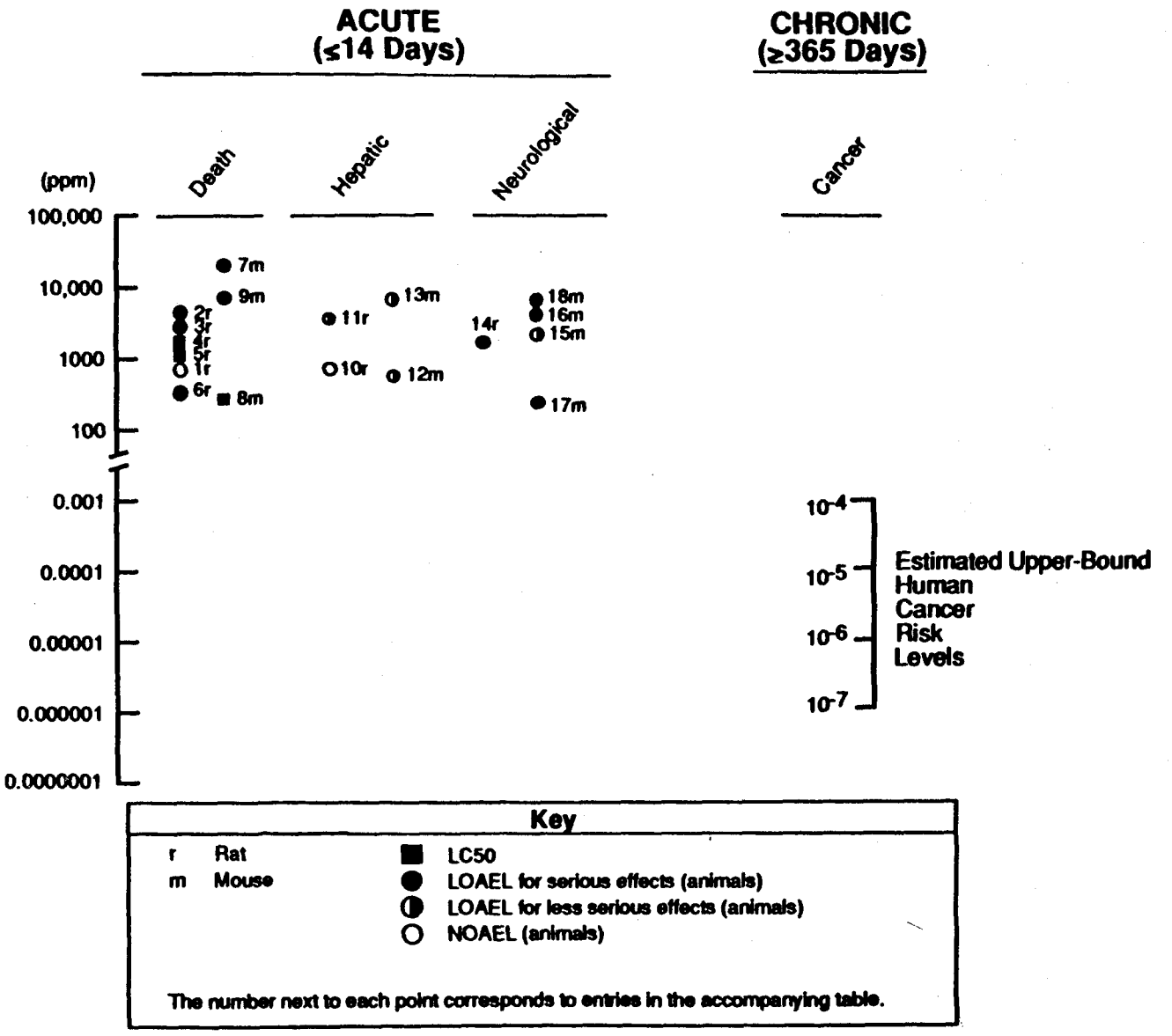


FIGURE 2-1. Levels of Significant Exposure to 1,1,2-Trichloroethane - Inhalation

lesions in the lungs, liver, or kidneys were found at autopsy. More than half of the test rats died following 7-hour exposure to 250 or 500 ppm of 1,1,2-trichloroethane, but no rats died following exposure to 100 ppm [Unpublished data, Dow Chemical Co. (cited in Torkelson and Rowe 198l)]. The results of this study were not used as levels of significant exposure because experimental methods and results were not described in sufficient detail. In rats exposed to 1,1,2-trichloroethane for 8 hours, the LC_{50} was 999 ppm (Pozzani et al. 1959). These authors reported, in a later study, that exposure to 500 ppm for 8 hours produced death in 4 out of 6 rats within 14 days (Smyth et al. 1969).

In mice, 12,934 ppm of 1,1,2-trichloroethane was found to be the minimum lethal concentration in a 2-hour exposure test (Lazarew 1929). The animals lay down on their sides and lost control of their reflexes prior to death. An LC_{50} value of 416 ppm was calculated in mice exposed for 6 hours and observed for 14 days (Gradiski et al. 1978). In mice exposed to 3750 ppm of 1,1,2-trichloroethane, the LT_{50}, or exposure duration that produced mortality in one-half of the mice tested, was calculated to be 600 minutes (Gehring 1968).

Only one study investigated the health effects of long-term inhalation exposure to 1,1,2-trichloroethane. Exposure to 15 ppm of 1,1,2-trichloroethane for 6 months did not increase mortality in rats, guinea pigs, or rabbits [Unpublished data, Dow Chemical Co. (cited in Torkelson and Rowe 1981)]. Values reported by this study are not included as levels of significant exposure because experimental methods and results were not described in sufficient detail.

The highest NOAEL values and all reliable LOAEL values for death in each species are recorded in Table 2-1 and plotted in Figure 2-1. The concentrations of 416 ppm (Gradiski et al. 1978) and 500 ppm (Smyth et al. 1969) in air are presented in Table 1-2.

2.2.1.2 Systemic Effects

Respiratory Effects. No studies were located regarding respiratory effects in humans following inhalation exposure to 1,1,2-trichloroethane.

Only one study investigated the respiratory effects of 1,1,2-trichloroethane inhalation in animals. Bonnet et al. (1980) macroscopically examined the lungs of rats that survived a 6-hour exposure test from which an LC_{50} of 1654 ppm was calculated. No lesions were found. This study was not used as the basis of a NOAEL because histological examinations were not performed, and gross observations alone are not sufficient to detect subtle health effects.

Hepatic Effects. No studies were located regarding hepatic effects in humans following inhalation exposure to 1,1,2-trichloroethane.

Several studies examined the hepatotoxicity of inhaled 1,1,2-trichloroethane vapor in animals. In rats, inhalation of 2080 ppm of 1,1,2-trichloroethane for 2 hours resulted in a small, but significant, increase in serum glutamic-pyruvic transaminase (SGPT) levels measured 22 hours after exposure ended (Carlson 1973). This treatment did not affect serum glutamic-oxaloacetic transaminase (SGOT), glucose-6-phosphatase, or liver weight. There were no hepatic effects after exposure to 890 ppm in this study. Macroscopic examination of rats that survived exposure to 250 ppm of 1,1,2-trichloroethane for 4 hours, and 250-500 ppm for 7 hours, revealed necrosis and tissue damage in the liver [Unpublished data, Dow Chemical Co. (cited in Torkelson and Rowe 1981)]. No macroscopic lesions were found in the livers of rats that survived a 6-hour exposure test from which an LC_{50} of 1654 ppm was calculated (Bonnet et al. 1980). This study was not used as the basis of a NOAEL because histological examinations were not performed, and gross observations alone are not sufficient to detect subtle health effects. The occurrence of hepatic effects at lower concentrations in the Dow Chemical study than in other studies may be due to differences in duration of exposure, endpoint examined, strain of rat used, or other differences in experimental protocols.

Mice exposed to 800 ppm of 1,1,2-trichloroethane for 3 hours had decreased adenosine triphosphate (ATP), increased liver triglycerides, decreased plasma triglycerides, and increased SGPT (Takahara 1986c). Recovery occurred within 20 hours for all parameters except SGPT, which remained elevated. The ET_{50} for increased SGPT levels in mice exposed to 3750 ppm of 1,1,2-trichloroethane (duration of exposure that produced increased SGPT levels in one-half of the exposed mice) was 17.5 minutes (Gehring 1968). This was substantially shorter than the LT_{50} of 600 minutes for lethality.

Minor fatty changes and cloudy swelling were found in the livers of female rats exposed to 30 ppm of 1,1,2-trichloroethane for 16 days. However, 6-month exposure to 15 ppm 1,1,2-trichloroethane did not have histopathological effects on the liver in rats, guinea pigs, or rabbits [Unpublished data, Dow Chemical Co. (cited in Torkelson and Rowe 1981)].

The highest NOAEL values and all reliable LOAEL values for hepatic effects in each species are recorded in Table 2-1 and plotted in Figure 2-l. Although increased SGPT is reported as a less serious effect, it is suggestive of cell damage that can range from less serious to serious. The study by Dow Chemical was not used as the basis of a NOAEL or LOAEL because experimental details were not reported. The concentration of 800 ppm in air (Takahara 1986c) is presented in Table 1-2.

Renal Effects. No studies were located regarding renal effects in humans following inhalation exposure to 1,1,2-trichloroethane.

The renal effects of 1,1,2-trichloroethane have been studied in animals. In the rat, inhalation of 250 ppm of 1,1,2-trichloroethane for 4

hours produced kidney necrosis [Unpublished data, Dow Chemical Co. (cited in Torkelson and Rowe 1981)]. Exposure to 250 or 500 ppm for 7 hours produced marked kidney damage. This study was not used as the basis of a LOAEL because experimental details were not reported. No macroscopic lesions were found in the kidneys of rats that survived a 6-hour exposure test from which an LC_{50} of 1654 ppm was calculated (Bonnet et al. 1980). This study was not used as the basis of a NOAEL because histological examinations were not performed, and gross observations alone are not sufficient to detect subtle health effects.

In the only long-term study available, 6-month exposure to 15 ppm of 1,1,2-trichloroethane did not produce renal histopathological effects in rats, guinea pigs, or rabbits [Unpublished data, Dow Chemical Co. (cited in Torkelson and Rowe 1981)]. This study was not used as the basis of a NOAEL because experimental details were not reported.

Other Systemic Effects. No studies were located regarding other systemic effects in humans following inhalation exposure to 1,1,2-trichloroethane.

One study examined the relationship between inhalation of 1,1,2-trichloroethane and body weight in animals. Reduced body weight gain was reported in rats following a 6-hour exposure test from which an LC_{50} of 1654 ppm was calculated (Bonnet et al. 1980). No level of significant exposure was taken from this study because no data were presented in the paper.

2.2.1.3 Immunological Effects

No studies were located regarding immunological effects in humans or animals following inhalation exposure to 1,1,2-trichloroethane.

2.2.1.4 Neurological Effects

No studies were located regarding neurological effects in humans following inhalation exposure to 1,1,2-trichloroethane.

Studies in animals indicate that inhalation of 1,1,2-trichloroethane may produce neurological effects. Exposure to 1654 ppm of 1,1,2-trichloroethane for 6 hours produced excitation, followed by sleepiness, in rats (Bonnet et al. 1980). Mice exposed to 1,1,2-trichloroethane vapor for 2 hours laid down on their sides at 1833 ppm, and lost control of their reflexes at 2749 ppm. These concentrations are substantially lower than the minimum lethal concentration of 12,934 ppm that was reported in this study, which suggests that 1,1,2-trichloroethane exhibited increased central nervous system depression in this study (Lazarew 1929). The ET_{50} for anesthesia in mice exposed to 3750 ppm (duration of exposure that produced anesthesia in one-half of the exposed mice) was 18 minutes (Gehring 1968). This was substantially shorter than the LT_{50} of 600 minutes for lethality, indicating significant CNS-depressant potency in this study. A 50%

elevation in the threshold for pentylenetetrazol-induced seizures of CNS function, occurred in mice after exposure to 418 ppm of 1,1,2-trichloroethane for 4 hours (De Ceaurriz et al. 1981). This effect may indicate depression of CNS function.

All reliable LOAEL values for neurological effects in each species are recorded in Table 2-1 and plotted in Figure 2-1. The concentration of 418 ppm in air (De Ceaurriz et al. 1981) is presented in Table 2-2.

2.2.1.5 Developmental Effects

No studies were located regarding developmental effects in humans or animals following inhalation exposure to 1,1,2-trichloroethane.

2.2.1.6 Reproductive Effects

No studies were located regarding reproductive effects in humans or animals following inhalation exposure to 1,1,2-trichloroethane.

2.2.1.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans or animals following inhalation exposure to 1,1,2-trichloroethane.

2.2.1.8 Cancer

No studies were located regarding cancer in humans or animals following inhalation exposure to 1,1,2-trichloroethane. Because 1,1,2-trichloroethane was carcinogenic to mice by the oral route in the NCI (1978) bioassay (Section 2.2.2.8), it is assumed that it is carcinogenic by inhalation, and the q_1^* for oral exposure was adopted as the q_1^* for inhalation (EPA 1988a). The q_1^* was converted to a unit risk for inhalation of 1.6×10^{-5} $(\mu/m^3)^{-1}$, which is equivalent to 8.7×10^{-2} $(ppm)^{-1}$. This unit risk corresponds to upper bound individual lifetime cancer risks at 10^{-4} to 10^{-7} of 1×10^{-3} to 1×10^{-6} ppm, which are plotted in Figure 2-1.

2.2.2 Oral Exposure

2.2.2.1 Death

No studies were located regarding death in humans following oral exposure to 1,1,2-trichloroethane.

Several reports indicate that 1,1,2-trichloroethane may be lethal to animals. An LD_{50} of 837 mg/kg (0.58 mL/kg) was calculated for orally administered, undiluted 1,1,2-trichloroethane in rats (Smyth et al. 1969). Moody et al. (1981) reported no mortality among fasted rats given single oral doses of 1,1,2-trichloroethane in mineral oil at 1080 mg/kg, but this value was not used as a NOAEL because only deaths during the first 18 hours

TABLE 2-2. Levels of Significant Exposure to 1,1,2-Trichloroethane - Oral

Graph Key	Species	Route[c]	Exposure Frequency/ Duration	Effect	NOAEL[b] (mg/kg/day)	LOAEL[a] (Effect) Less Serious (mg/kg/day)	LOAEL[a] (Effect) Serious (mg/kg/day)	Reference
ACUTE EXPOSURE								
Lethality								
1	rat	(G)	1x				837 (LD_{50})	Smyth et al. 1969
2	mouse	(G)	1x				378 (LD_{50})	White et al. 1985
3, 4	mouse	(G)	1x/d 7 d		100		300 (7/7 dead)	Kallman et al. 1983
5, 6	dog		1x		433		722 (1/1 dead)	Wright and Schaffer 1932
Systemic								
7	rat	(G)	1x	Hepatic		1080 (biochemical changes)		Moody and Smuckler Smuckler 1986
8	rat	(G)	1x	Hepatic		1080 (biochemical changes)		Moody et al. 1981 1981
9	rat	(G)	1x	Hepatic		60 (incr SGOT and SGPT)		Tyson et al. 1983
10	rat	(G)	1x/d	Hepatic		180 (biochemical changes)		Platt and Cockrill 1969
11			7 d	Other		180 (body wt changes)		
12	mouse	(G)	1x/d	Hemato	38			White et al. 1985
13			14 d	Hepatic	38			
14				Renal	38			
15				Other	38			
16, 17	dog		1x	Gastro		144 (mild effect)	433 (hemorrhage)	Wright and Schaffer 1932
18, 19				Hepatic		144 (mild effect)	433 (necrosis)	
20				Renal		144 (mild effect)		

TABLE 2-2 (continued)

Graph Key	Species	Route[c]	Exposure Frequency/ Duration	Effect	NOAEL[b] (mg/kg/day)	LOAEL[a] (Effect)		Reference
						Less Serious (mg/kg/day)	Serious (mg/kg/day)	
Immunological								
21	mouse	(G)	1x/d 14 d		38			Sanders et al. 1985
Neurological								
22	mouse	(G)	1x				450 (sedation)	White et al. 1985
23	mouse	(G)	1x				128 (motor impairment)	Borzelleca 1983
24,25	mouse	(G)	1x/d 7 d		30[d]	100 (taste aversion)		Kallman et al. 1983
26	mouse	(W)	4d		46			Kallman and Kaempf 1984
27, 28	dog		1x		144		289 (drowsiness)	Wright and Schaffer 1932
Reproductive								
29	mouse	(G)	5d (days 8-12 of gestation)		350			Seidenberg et al. 1986
INTERMEDIATE EXPOSURE								
Systemic								
30	rat	(G)	5 d/wk 7 wk	Other		69 (body wt changes)		Story et al. 1986
31	mouse	(W)	90 d	Hemato	305			White et al. 1985
32, 33				Hepatic	4.4[e]	46 (liver effects)		
34				Renal	305			
35, 36				Other	46	305 (body wt changes)		

TABLE 2-2 (continued)

Graph Key	Species	Route[c]	Exposure Frequency/ Duration	Effect	NOAEL[b] (mg/kg/day)	LOAEL[a] (Effect) Less Serious (mg/kg/day)	LOAEL[a] (Effect) Serious (mg/kg/day)	Reference
Immunological								
37,38	mouse	(W)	90 d		4.4	44 (immune effects)		Sanders et al. 1985
CHRONIC EXPOSURE								
Lethality								
39	rat	(G)	5 d/wk 78 wk		92			NCI 1978
40	mouse	(G)	5 d/wk 78 wk				195 (increased mortality)	NCI 1978
Systemic								
41	rat	(G)	5 d/wk 78 wk	Resp	92			NCI 1978
				Cardio	92			
				Gastro	92			
				Hemato	92			
				Musc/skel	92			
				Hepatic	92			
				Renal	92			
				Derm/Oc	92			
				Other	92			
42	mouse	(G)	5 d/wk 78 wk	Resp	390			NCI 1978
				Cardio	390			
				Gastro	390			
				Hemato	390			
				Musc/skel	390			
				Hepatic	390			
				Renal	390			
				Derm/Oc	390			
				Other	390			

TABLE 2-2 (continued)

Graph Key	Species	Route[c]	Exposure Frequency/ Duration	Effect	NOAEL[b] (mg/kg/day)	LOAEL[a] (Effect)		Reference
						Less Serious (mg/kg/day)	Serious (mg/kg/day)	
Carcinogenic								
43	mouse	(G)	5 d/wk 78 wk				195 (CEL[f]-liver, adrenals)	NCI 1978

[a]LOAEL - Lowest Observed Adverse Effect Level
[b]NOAEL - No Observed Adverse Effect Level
[c]G - gavage, W - drinking water
[d]Used to derive acute oral MRL; dose divided by an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability) resulting in an MRL of 0.3 mg/kg/day. The MRL was converted to an equivalent concentration in water (10.5 ppm) for presentation in Table 1-3.
[e]Used to derive intermediate oral MRL; dose divided by an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability) resulting in an MRL of 0.04 mg/kg/day. The MRL was converted to an equivalent concentration in water (1.4 ppm) for presentation in Table 1-3.
[f]CEL - Cancer Effect Level

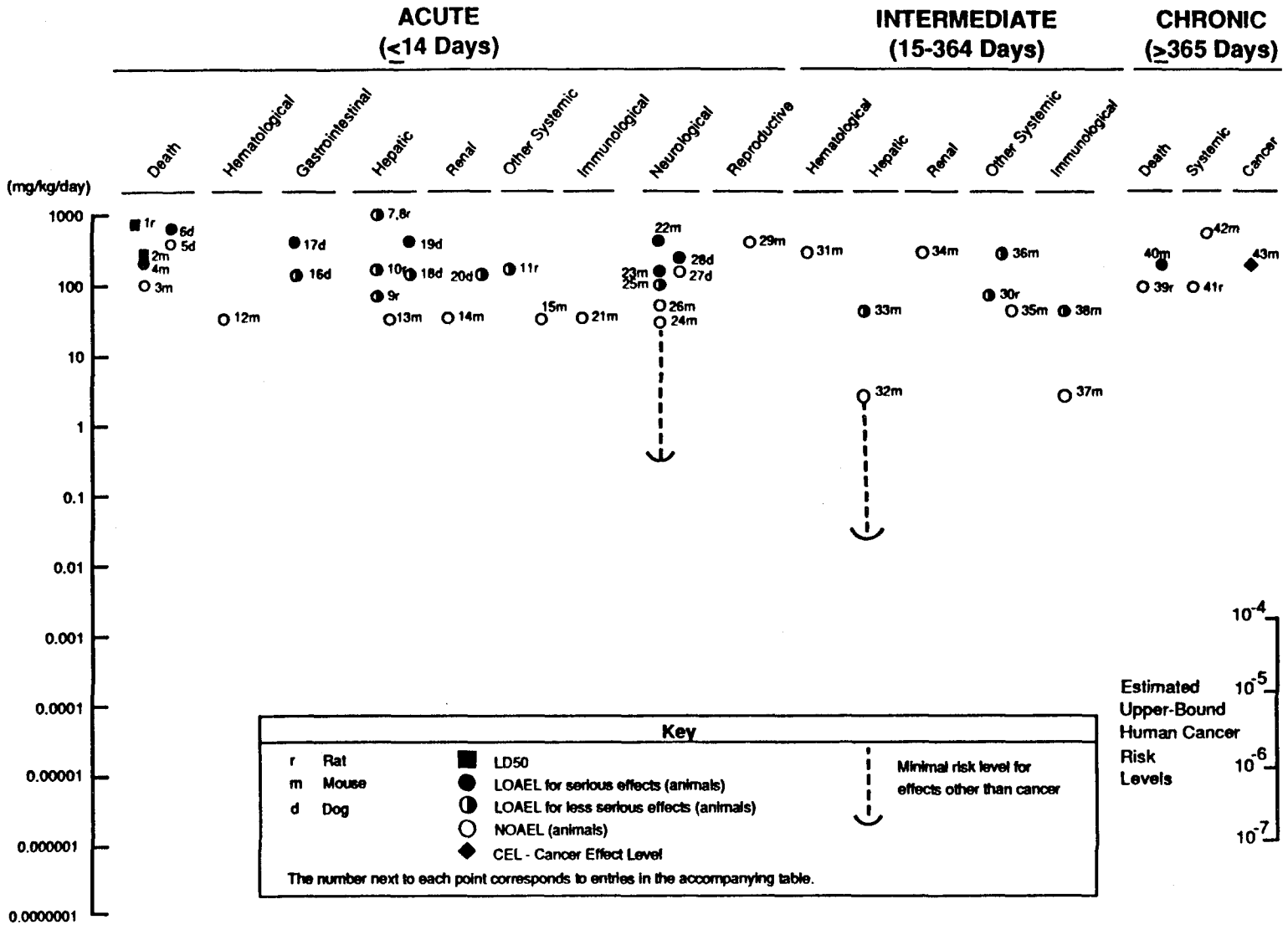


FIGURE 2-2. Levels of Significant Exposure to 1,1,2-Trichloroethane - Oral

after administration were recorded, and only 3 rats were tested. In mice, the oral LD_{50} of 1,1,2-trichloroethane administered by gavage in water was reported to be 378 mg/kg for males and 491 mg/kg for females (White et al. 1985). The lower value of 378 mg/kg, which was obtained in the males, was used in Table 2-2 and Figure 2-2. Necropsy of mice that died in this study revealed hemorrhagic areas in the lungs and pale coloration of the liver, which may also have been caused by hemorrhage. These effects may have contributed to the death of these animals. The only dog given 1,1,2-trichloroethane (vehicle not specified) at 722 mg/kg died, but all 5 that received doses ranging from 144 to 433 mg/kg survived (Wright and Schaffer 1932).

Lethality was investigated in two short-term repeated-dose studies. Oral doses of 1,1,2-trichloroethane given by gavage in water at 300 mg/kg, repeated daily for 7 days, resulted in the death of all 7 mice tested (Kallman et al. 1983). Doses up to 100 mg/kg/day did not produce death in this study. Oral administration by gavage of 38 mg/kg/day in 10% Emulphor for 14 days did not produce mortality in mice (White et al. 1985).

One long-term study investigated the effect of 1,1,2-trichloroethane on animal survival. Mice were given daily oral doses of 1,1,2-trichloroethane at 195 or 390 mg/kg in corn oil for 78 weeks (NCI 1978). Although male survival was not affected, female survival was reduced in a dose-dependent manner. A large number of the deaths in the female low dose group occurred early in the experiment; these were not tumor-related and did not appear to have a common cause. In rats, survival was not affected by oral administration of doses of 1,1,2-trichloroethane at either 46 or 92 mg/kg/day for 78 weeks (NCI 1978). However, rat vehicle controls had unusually high mortality in this study.

The highest NOAEL values and all reliable LOAEL values for death in each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2. No short-term studies of 1,1,2-trichloroethane administered in drinking water were located; therefore the dose level of 837 mg/kg/day, which was administered by gavage undiluted (Smyth et al. 1969), and the dose level of 378 mg/kg/day, which was administered by gavage in water (White et al. 1985), were converted to equivalent concentrations, respectively, of 5980 and 1990 ppm in water for presentation in Table l-4. No long-term studies of 1,1,2-trichloroethane administered in food were located; therefore the dose level of 195 mg/kg/day, which was administered by gavage in corn oil (NCI 1978), was converted to an equivalent concentration of 1500 ppm in food for presentation in Table l-4.

2.2.2.2 Systemic Effects

Respiratory Effects. No studies were located regarding respiratory effects in humans following oral exposure to 1,1,2-trichloroethane.

Respiratory effects have been studied in animals. Hemorrhagic areas were found in the lungs of mice that died following gavage administration of 1,1,2-trichloroethane in water at 200 to 600 mg/kg (White et al. 1985). This study was not used as the basis of a LOAEL because the effect was reported only in mice that died as a result of exposure. Daily administration of 1,1,2-trichloroethane by gavage in 10% Emulphor at 38 mg/kg for 14 days did not affect lung weight in the mouse (White et al. 1985). Consumption of 305 mg/kg/day by males and 384 mg/kg/day by females in the drinking water for 90 days was also without effect on mouse lung weight (White et al. 1985). These dose levels were not used as NOAEL values because lung weight alone may not be an adequate endpoint to assess possible tissue damage. However, organ weight changes, when they occur in conjunction with other subtle effects, may indicate tissue damage. Histopathological examination of respiratory organs and tissues using light microscopy found no increase in the occurrence of non-neoplastic lesions following 78 weeks of oral 1,1,2-trichloroethane administration in corn oil at doses of 46 or 92 mg/kg/day in rats and 195 or 390 mg/kg/day in mice (NCI 1978). NOAEL values for respiratory effects derived from this study are recorded in Table 2-2 and plotted in Figure 2-2.

Cardiovascular Effects. No studies were located regarding cardiovascular effects in humans following oral exposure to 1,1,2-trichloroethane.

One study of cardiovascular effects in animals was located. Histopathological examination of cardiovascular tissues using light microscopy found no increase in the occurrence of non-neoplastic lesions following 78 weeks of oral 1,1,2-trichloroethane administration in corn oil at doses of 46 or 92 mg/kg/day in rats and 195 or 390 mg/kg/day in mice (NCI 1978). NOAEL values for cardiovascular effects in each species are recorded in Table 2-2 and plotted in Figure 2-2.

Gastrointestinal Effects. No studies were located regarding gastrointestinal effects in humans following oral exposure to 1,1,2-trichloroethane.

There is some evidence for adverse gastrointestinal effects in animals. Mice that died following administration by gavage in water of single oral doses of 1,1,2-trichloroethane above 200 mg/kg displayed a dose-related increase in the incidence of gastric irritation until all animals were affected at 500 mg/kg (White et al. 1985). This study was not used as the basis of a LOAEL because the effect was reported only in mice that died as a result of exposure. Mild inflammation and congestion of the gastrointestinal tract, as well as nausea, were noted in a dog given oral administration (vehicle not specified) of 144 mg/kg (Wright and Schaffer 1932). Severe irritation and hemorrhage were found in 2 of the 3 dogs given doses of 433 or 722 mg/kg. Histopathological examination of gastrointestinal organs and tissues by light microscopy revealed no increase in the occurrence of non-neoplastic lesions following 78 weeks of oral

1,1,2-trichloroethane administration by gavage in corn oil at doses of 46 or 92 mg/kg/day in rats and 195 or 390 mg/kg/day in mice (NCI 1978). The highest NOAEL values and all reliable LOAEL values for gastrointestinal effects in each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2.

Hematological Effects. No studies were located regarding hematological effects in humans following oral exposure to 1,1,2-trichloroethane.

In animals, hematological effects were the subject of several studies. No hematological effects were found after daily administration to mice of 1,1,2-trichloroethane by gavage in Emulphor at 38 mg/kg for 14 days (White et al. 1985). No hematological effects were found in male mice exposed to ≤305 mg/kg/day in the drinking water for 90 days, but changes in hematological parameters were recorded in females that received doses as low as 3.9 mg/kg/day (White et al. 1985). These included mild decreases in hematocrit and hemoglobin at 384 mg/kg/day, increases in platelets and fibrinogen that were found in all groups, but were not dose-related, and leukocytes that were elevated, compared to controls, in the high-dose group, but which were only slightly higher than the historical control value in this laboratory. There was also a decrease in prothrombin time that appeared to be dose-related and became significant at 44 mg/kg/day. These changes were not clearly adverse to the mice, so only a NOAEL was derived from this study. Histopathological examination of spleen and bone marrow using light microscopy found no increase in the occurrence of non-neoplastic lesions following 78 weeks of oral 1,1,2-trichloroethane administration in corn oil at doses of 46 or 92 mg/kg/day in rats and 195 or 390 mg/kg/day in mice (NCI 1978). The NOAEL values for hematological effects in each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2.

Musculoskeletal Effects. No studies were located regarding musculoskeletal effects in humans following oral exposure to 1,1,2-trichloroethane.

Only one study investigated musculoskeletal effects in animals. Histopathological examination of musculoskeletal tissues by light microscopy revealed no increase in the occurrence of non-neoplastic lesions following 78 weeks of oral 1,1,2-trichloroethane administration in corn oil at doses of 46 or 92 mg/kg/day in rats and 195 or 390 mg/kg/day in mice (NCI 1978). NOAEL values for musculoskeletal effects in each species are recorded in Table 2-2 and plotted in Figure 2-2.

Hepatic Effects. No studies were located regarding hepatic effects in humans following oral exposure to 1,1,2-trichloroethane.

Necropsy of mice that died following single oral doses of 1,1,2-trichloroethane by gavage in water at 200 to 600 mg/kg revealed pale coloration of the liver (White et al. 1985). This study was not used as the basis of a LOAEL because the effect was reported only in mice that died as a

result of exposure. Dogs given 144 mg/kg or more had congestion, fatty degeneration, edema, and the onset of necrosis in the liver (Wright and Schaffer 1932). Massive liver necrosis occurred in 1 of the 3 dogs given 433 mg/kg or above. Tyson et al. (1983) found significant increases in SGOT and SGPT following oral administration of 1,1,2-trichloroethane in corn oil to rats. The ED_{50} for this effect was 60 mg/kg. Decreases in cytochrome P-450, ALA-dehydratase, and glutathione levels occurred after administration of 1080 mg/kg by gavage in mineral oil in rats (Moody et al. 1981, Moody and Smuckler 1986). Increased relative liver weight and alterations in fatty acid content of liver microsomes (increased oleic acid and decreased arachidonic acid content) were also seen in this study, which was limited by small sample size (Moody et al. 1981). Glucose-6-phosphate dehydrogenase levels increased 195%, and $NADH_2$-cytochrome c reductase levels decreased 33%, in rats administered 1,1,2-trichloroethane orally in liquid paraffin at 180 mg/kg/day for 7 days (Platt and Cockrill 1969). Liver weight, microsomal and cell-sap protein concentrations, and levels of $NADPH_2$-cytochrome c reductase, aminopyrine demethylase, glucose-6-phosphatase, lactate dehydrogenase, glutamate dehydrogenase, and 6-phosphogluconate dehydrogenase were not significantly changed in this study. SGPT levels were not affected by 14-day administration of 1,1,2-trichloroethane by gavage in an aqueous Emulphor emulsion at 38 mg/kg/day in mice (White et al. 1985). In male mice exposed to 1,1,2-trichloroethane for 90 days in the drinking water, liver glutathione decreased 16% following exposure to 46 mg/kg/day and 28% following exposure to 305 mg/kg/day; serum transaminase levels were not significantly increased at either dose (White et al. 1985). In the same study, female mice that received 384 mg/kg/day had a 13% increase in liver glutathione and significantly elevated SGPT levels. SGOT levels were increased in females exposed to 3.9 mg/kg/day and above, but this was not considered to be a compound-related effect because no dosedependency was established. The NOAEL for liver effects in this study was taken to be 4.4 mg/kg/day. Based on this value, which was rounded off to 4mg/kg/day, an intermediate oral MRL of 0.04 mg/kg/day was calculated, as described in the footnote in Table 2-2. This MRL has been converted to an equivalent concentration in water (1.4 ppm) for presentation in Table 1-3. No increase in the occurrence of non-neoplastic lesions in the liver was found by light microscopic histopathological examination following 78 weeks of oral 1,1,2-trichloroethane administration by gavage in corn oil at doses of 92 mg/kg/day in rats and 390 mg/kg/day in mice (NCI 1978).

The highest NOAEL values and all reliable LOAEL values for hepatic effects in each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2. No short-term studies of 1,1,2-trichloroethane administered in food were located; therefore, the dose level of 60 mg/kg/day, which was administered by gavage in corn oil (Tyson et al. 1983), was converted to an equivalent concentration of 1200 ppm in food for presentation in Table 1-4. The dose of 46 mg/kg/day was calculated from an administered concentration of 200 ppm in water (White et al. 1985). This concentration is presented in Table 1-4.

Renal Effects. No studies were located regarding renal effects in humans following oral exposure to 1,1,2-trichloroethane.

There are some reports of renal toxicity in animals, although most studies reported negative results. Cloudy swelling and congestion of the kidney were found by histopathological examination in dogs given 1,1,2-trichloroethane orally (vehicle not specified) at doses of 144 mg/kg or above (Wright and Schaffer 1932). There was a significant, low-level depression of in vitro organic ion uptake in renal cortical slices taken from rats given single oral doses of 1,1,2-trichloroethane in corn oil at 72 to 505 mg/kg (Watrous and Plaa 1972a). There was no clear dose-response relationship in this study, however. In mice administered 1,1,2-trichloroethane at up to 2886 mg/kg, the results were more inconsistent, with significant increases and decreases reported at various doses in different trials (Watrous and Plaa 1972a). Consequently, this study was not used as the source of a level of significant exposure in either species. There were no significant changes in kidney weight or blood urea nitrogen, an indicator of kidney function, in mice given 1,1,2-trichloroethane by gavage in 10% Emulphor for 14 days at a dose of 38 mg/kg/day or in the drinking water for 90 days at a dose of 305 mg/kg/day in males and 384 mg/kg/day in females (White et al. 1985). No increase in the occurrence of non-neoplastic lesions was found in the kidney by light microscopic histopathological examination following 78 weeks of oral 1,1,2-trichloroethane administration in corn oil at doses of 92 mg/kg/day in rats and 390 mg/kg/day in mice (NCI 1978). The highest NOAEL values and all reliable LOAEL values for renal effects in each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2.

Dermal/Ocular Effects. No studies were located regarding dermal or ocular effects in humans following oral exposure to 1,1,2-trichloroethane.

Only one study evaluated dermal or ocular effects in animals. Histopathological examination of the skin and eye using light microscopy found no increase in the occurrence of non-neoplastic lesions following 78 weeks of oral 1,1,2-trichloroethane administration in *corn oil at* doses of 46 or 92 mg/kg/day in rats and 195 or 390 mg/kg/day in mice (NCI 1978). NOAEL values for dermal/ocular effects in each species are recorded in Table 2-2 and plotted in Figure 2-2.

Other Systemic Effects. No studies were located regarding other systemic effects in humans following oral exposure to 1,1,2-trichloroethane.

The effect of 1,1,2-trichloroethane on body weight was investigated in several reports. Moody et al. (1981) reported reduced body weight gain in rats orally exposed to 1,1,2-trichloroethane in mineral oil at 1080 mg/kg, but a LOAEL was not derived because no data were presented. Rats given 180 mg/kg/day in liquid paraffin for 7 days grew only 8% over the course of the experiment, whereas control rats grew 34% (Platt and Cockrill 1969). Growth was reduced approximately 60% in rats given 69 mg/kg/day by gavage in corn

oil for 7 weeks (Story et al. 1986). In mice, body weight gain was not significantly affected by gavage administration of 1,1,2-trichloroethane in 10% Emulphor at 38 mg/kg/day for 14 days (White et al. 1985). Kallman and Kaempf (1984) reported that body growth in male mice was unchanged by go-day exposure to 46 mg/kg/day in the drinking water. Exposure to 1,1,2-trichloroethane in the drinking water for 90 days produced a concentration-dependent reduction in weight gain in male mice that was significant at 305 mg/kg/day (White et al. 1985). Weight gain in female mice was not affected in this study. When administered by gavage in corn oil, doses of 92 mg/kg/day in rats and 390 mg/kg/day in mice for 78 weeks (NCI 1978) did not inhibit body growth. The highest NOAEL and all reliable LOAEL values for reduced growth in each species and duration category are recorded in Table 2-2 and plotted in Figure 2-2. Some of the variability in these results may be explained by differences in the vehicles and animal strains used.

2.2.2.3 Immunological Effects

No studies were located regarding immunological effects in humans following oral exposure to 1,1,2-trichloroethane.

Immunological effects in mice were studied by Sanders and co-workers (Sanders et al. 1985, White et al. 1985). Oral administration of 1,1,2-trichloroethane to male mice at gavage doses in 10% Emulphor up to 38 mg/kg once a day for 14 days had no effect on humoral or cell-mediated immune response to sheep red blood cells (Sanders et al. 1985). Humoral immune response was measured by the number of IgM antibody forming cells produced against sheep red blood cells in the spleen. Spleen and thymus weight were not affected by treatment (White et al. 1985). A NOAEL of 38 mg/kg/day for immunological effects in mice following acute oral exposure was derived from this study.

In a longer-term study, mice were exposed to 1,1,2-trichloroethane in the drinking water for 90 days (Sanders et al. 1985, White et al. 1985). Males received doses of 4.4, 46, and 305 mg/kg/day and females received doses of 3.9, 44, and 384 mg/kg/day. Humoral immune response was measured by the number of IgM antibody forming cells produced against sheep red blood cells in the spleen, hemagglutination titers, and spleen lymphocyte response to lipopolysaccharide (Sanders et al. 1985). The number of antibody forming cells in the spleen was not consistently affected by treatment. A significant increase was obtained in females that received 384 mg/kg/day, but only on day 4 following immunization and only when counted on a 10^6 cell basis. Significant increases were also found by some measurements in low-dose males, but high-dose males were not affected. Hemaglutination titers exhibited a dose-dependent depression that was significant at 46 mg/kg/day in males

Cell-mediated immune response to sheep red blood cells was not affected in any group tested by Sanders et al. (1985). Both delayed-type hypersensitivity and popliteal lymph node proliferation responses were examined. Other immune responses were also evaluated. Peritoneal macrophages from males exposed to 305 mg/kg/day had a significantly depressed ability to phagocytize sheep red blood cells. This effect was not found in females. The functional activity of the fixed macrophages of the reticuloendothelial system was altered in females exposed to 384 mg/kg/day, which had a 17% increase in vascular clearance of sheep red blood cells, but not males. Spleen weight was unchanged in most groups, but was increased in females exposed to 384 mg/kg/day (White et al. 1985). Thymus weight was not affected in any group.

On the basis of this study, 44 mg/kg was chosen as the LOAEL and 4.4 mg/kg/day as the NOAEL for immunological effects in oral studies of intermediate duration. The dose of 44 mg/kg/day was calculated from an administered concentration of 200 ppm in water by Sanders et al. (1985). This concentration is presented in Table l-4.

No increase in the occurrence of non-neoplastic lesions was found in organs and tissues of the immune system following 78 weeks of oral 1,1,2-trichloroethane administration in corn oil at doses of 46 or 92 mg/kg/day in rats and 195 or 390 mg/kg/day in mice (NCI 1978). This study involved histopathological examination of the spleen, thymus, and lymph nodes using light microscopy, but because specific tests for immunotoxicity were not performed, NOAEL values were not derived.

2.2.2.4 Neurological Effects

No studies were located regarding neurological effects in humans following oral exposure to 1,1,2-trichloroethane.

1,1,2-Trichloroethane has neurological effects in acutely exposed animals. All mice given single oral doses of 1,1,2-trichloroethane at 450 mg/kg or more in water were sedated within 1 hour of administration (White et al. 1985). The ED_{50} for motor impairment (dose that produced motor impairment in one half of the test animals) in mice was 128 mg/kg administered by gavage in water (Borzelleca 1983). The peak effect occurred within 5 minutes of exposure. In dogs, doses of 1,1,2-trichloroethane at 289 to 722 mg/kg (vehicle not specified) produced drowsiness, incoordination, and partial narcosis after 12 to 50 minutes (Wright and Schaffer 1932).

Kallman et al. (1983) reported that 1,1,2-trichloroethane administered by gavage in water produced a significant dose-related taste aversion to saccharin in the drinking water. The NOAEL for this effect was 30 mg/kg and the LOAEL was 100 mg/kg. An ED_{50} of 32 mg/kg was calculated. Mice did not

display a taste aversion to 1,1,2-trichloroethane itself when 46 mg/kg/day was added to the drinking water for 4 days (Kallman and Kaempf 1984).

Longer-term studies did not report neurological effects following oral administration of 1,1,2-trichloroethane. Administration of 38 mg/kg/day in 10% Emulphor for 14 days did not affect brain weight in mice (White et al. 1985). Mouse brain weight was also unaffected by exposure to 305-384 mg/kg/day in the drinking water for 90 days (White et al. 1985). NOAEL values were not derived from these studies because brain weight alone is not an adequate endpoint to assess neurotoxicity. No effect on the occurrence of non-neoplastic lesions in nervous system organs and tissues was found by histopathological examination using light microscopy following 78 weeks of oral 1,1,2-trichloroethane administration in corn oil at doses of 46 or 92 mg/kg/day in rats and 195 or 390 mg/kg/day in mice (NCI 1978). NOAEL values were not derived from this study because tests of nervous system function were not included, and histopathology alone may not be an adequate endpoint to assess neurotoxicity.

The highest NOAEL values and all reliable LOAEL values for neurological effects in each species are recorded in Table 2-2 and plotted in Figure 2-2. Effects were not reported by short-term studies of 1,1,2-trichloroethane in drinking water; therefore, the dose levels of 100 mg/kg/day, resulting in taste aversion (Kallman et al. 1983), and 128 mg/kg/day, resulting in motor impairment (Borzelleca 1983), which were administered by gavage in water, were converted to equivalent concentrations of 525 and 670 ppm, respectively, for presentation in Table 1-4. Based on the NOAEL of 30mg/kg/day, an acute oral MRL of 0.3 mg/kg/day was calculated as described in the footnote in Table 2-2. This MRL has been converted to an equivalent NOAEL of 30 concentration in water (10.5 ppm) for presentation in Table l-3.

2.2.2.5 Developmental Effects

No studies were located regarding developmental effects in humans following oral exposure to 1,1,2-trichloroethane.

One study of the developmental effects of 1,1,2-trichloroethane in animals was found. Pregnant female mice were orally administered 1,1,2-trichloroethane in corn oil at 350 mg/kg/day on days 8 through 12 of gestation (Seidenberg et al. 1986). The percent survival of neonates from day 1 through day 3 was not affected by treatment, and neither was average neonatal weight measured on days 1 and 3 post partum. A NOAEL for developmental effects was not derived from this study because more explicit developmental endpoints (eg the incidence of malformations) were not investigated.

2.2.2.6 Reproductive Effects

No studies were located regarding reproductive effects in humans following oral exposure to 1,1,2-trichloroethane.

Studies of orally administered 1,1,2-trichloroethane did not report significant reproductive effects in animals. Seidenberg et al. (1986) found no effect on number of litters resorbed or average number of neonates per litter in mice following oral administration of 350 mg/kg/day in corn oil on days 8 through 12 of gestation. This was a minimally toxic dose expected to produce significant maternal weight reduction and up to 10% maternal mortality. Maternal body weight was not affected in this study, but some maternal mortality did occur. A NOAEL of 350 mg/kg/day derived from this study is recorded in Table 2-2 and plotted in Figure 2-2. Testis weight in mice was not affected when 1,1,2-trichloroethane was administered by gavage in 10% Emulphor for 14 days at a dose of 38 mg/kg/day (White et al. 1985). Exposure to 46 mg/kg/day or above in the drinking water for 90 days produced a significant increase in relative, but not absolute, testis weight in mice (White et al. 1985). NOAEL and LOAEL values were not derived from these studies, however, because testes weight alone may not be an adequate endpoint to assess reproductive toxicity. Also, changes in testis weight are not necessarily associated with reproductive dysfunction. No effect on the occurrence of non-neoplastic lesions in structures of the reproductive system was found by histopathological examination using light microscopy following 78 weeks of oral 1,1,2-trichloroethane administration in corn oil at doses of 46 or 92 mg/kg/day in rats and 195 or 390 mg/kg/day in mice (NCI 1978). NOAEL values were not derived from this study because tests of reproductive function were not included and histopathology alone may not be an adequate endpoint to assess reproductive toxicity.

2.2.2.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans or animals following oral exposure to 1,1,2-trichloroethane.

2.2.2.8 Cancer

No studies were located regarding cancer in humans following oral exposure to 1,1,2-trichloroethane.

One study of cancer in animals orally exposed to 1,1,2-trichloroethane was located. There was no significant increase in the occurrence of neoplasms in Osbourne-Mendel rats of either sex following 78 weeks of oral 1,1,2-trichloroethane administration in corn oil at doses of 46 or 92 mg/kg/day (NCI 1978). In B6C3Fl mice, there was a highly significant dose-related increase in the incidence of hepatocellular carcinomas in both males and females following 78 weeks of oral administration in corn oil at doses of 195 or 390 mg/kg/day (NCI 1978). These carcinomas were found in 10 percent of untreated control males, 12 percent of vehicle control males, 37 percent of low-dose males, and 76 percent of high-dose males; they were found in 10 percent of untreated control females, 0% of vehicle control females, 33% of low-dose females, and 89% of high-dose females. In addition, there was a significant increase in the occurrence of adrenal

pheochromocytomas in mice of both sexes at 390 mg/kg/day. These lesions, not found in the control or low-dose groups, had an incidence of 17 percent in high-dose males and 28 percent in high-dose females. The value of this study is limited by its relatively short duration of 78 weeks and its conduct before the implementation of Good Laboratory Practices (GLP). A Cancer Effect Level (CEL) of 195 mg/kg/day is recorded in Table 2-2 and plotted in Figure 2-2. A ql* of 5.73×10^{-2} $(mg/kg/day)^{-1}$ was calculated for 1,1,2-trichloroethane based on the incidence of hepatocellular carcinoma in male mice (EPA 1980, 1988a). This q_1* was used to calculate upper bound individual lifetime cancer risks at 10^{-4} to 10^{-7} risk levels of 1.8×10^{-3} to $1.8 \times l0^{-6}$ mg/kg/day, which are plotted in Figure 2-2.

2.2.3 Dermal Exposure

2.2.3.1 Death

No studies were located regarding death in humans following dermal exposure to 1,1,2-trichloroethane.

Dermally applied 1,1,2-trichloroethane has been reported to cause death in animals. A single dermal application of 116 mg/cm^2 (0.25 mL applied to a 3.1 cm2 area of the back) was allowed to remain on the skin of guinea pigs until it disappeared (5 to 7 days). This treatment resulted in the death of 25% of the guinea pigs tested within 28 days (Wahlberg 1976). Doses of 233 and 931 mg/cm^2 killed all tested animals within 3 days in this study. A dose of 116 mg/cm^2 is, therefore, indicated as a LOAEL in Table 2-3 and Figure 2-3 for acute dermal exposure to 1,1,2-trichloroethane in guinea pigs. A dermal LD_{50} of 3.73 mL/kg (see Table 2-3) was reported for rabbits (Smyth et al. 1969). This value could not be plotted in Figure 2-3 because it was not reported in per-area units.

2.2.3.2 Systemic Effects

Hepatic Effects. No studies were located regarding hepatic effects in humans following dermal exposure to 1,1,2-trichloroethane.

One study investigated the hepatotoxicity of dermally applied 1,1,2-trichloroethane in animals. Guinea pig liver glycogen content was reduced within 2 hours following dermal application of 1 mL of 1,1,2-trichloroethane to a 3.1 cm^2 area of the back (465 mg/cm^2) (Kronevi et al. 1977). Hydropic changes in the liver were also found. These effects may not have been compound-related, however, since they were found in animals killed under anesthesia produced by pentobarbital, but not unanesthetized animals. Untreated controls were not used in this study. The authors suggest that these liver effects may be due to an interaction between 1,1,2-trichloroethane and pentobarbital. This possibility is discussed further in Section 2.7.

TABLE 2-3. Levels of Significant Exposure to 1,1,2-Trichloroethane - Dermal

Graph Key	Species	Exposure Frequency/ Duration	Effect	NOAEL	LOAEL[a] (Effect)		Reference
					Less Serious	Serious	
ACUTE EXPOSURE							
Lethality							
1	guinea pig	5-7 d				116 mg/cm^2/day (5/20 dead)	Wahlberg 1976
	rabbit	1x				3.73 mL/kg (LD_{50})	Smyth et al. 1969
Systemic							
2	human	5 min	Derm/Oc		698 mg/cm^2 (stinging pain)		Wahlberg 1984a
	human	5 min	Derm/OC	0.1 mL			Wahlberg 1984a
3	guinea pig	12 h	Derm/Oc		465 mg/cm^2 (skin damage)		Kronevi et al. 1977
4			Renal	465 mg/cm^2			
	rabbit	24 h	Derm/Oc	0.01 mL			Smyth et al. 1969
	rabbit	10 d 1x/d	Derm/Oc		0.1 mL (irritation)		Wahlberg 1984b
INTERMEDIATE EXPOSURE							
Systemic							
	human	15 d 1x/d	Derm/Oc	0.1 ML			Wahlberg 1984b

[a]LOAEL - Lowest Observed Adverse Effect Level
[b]NOAEL - No Observed Adverse Effect Level

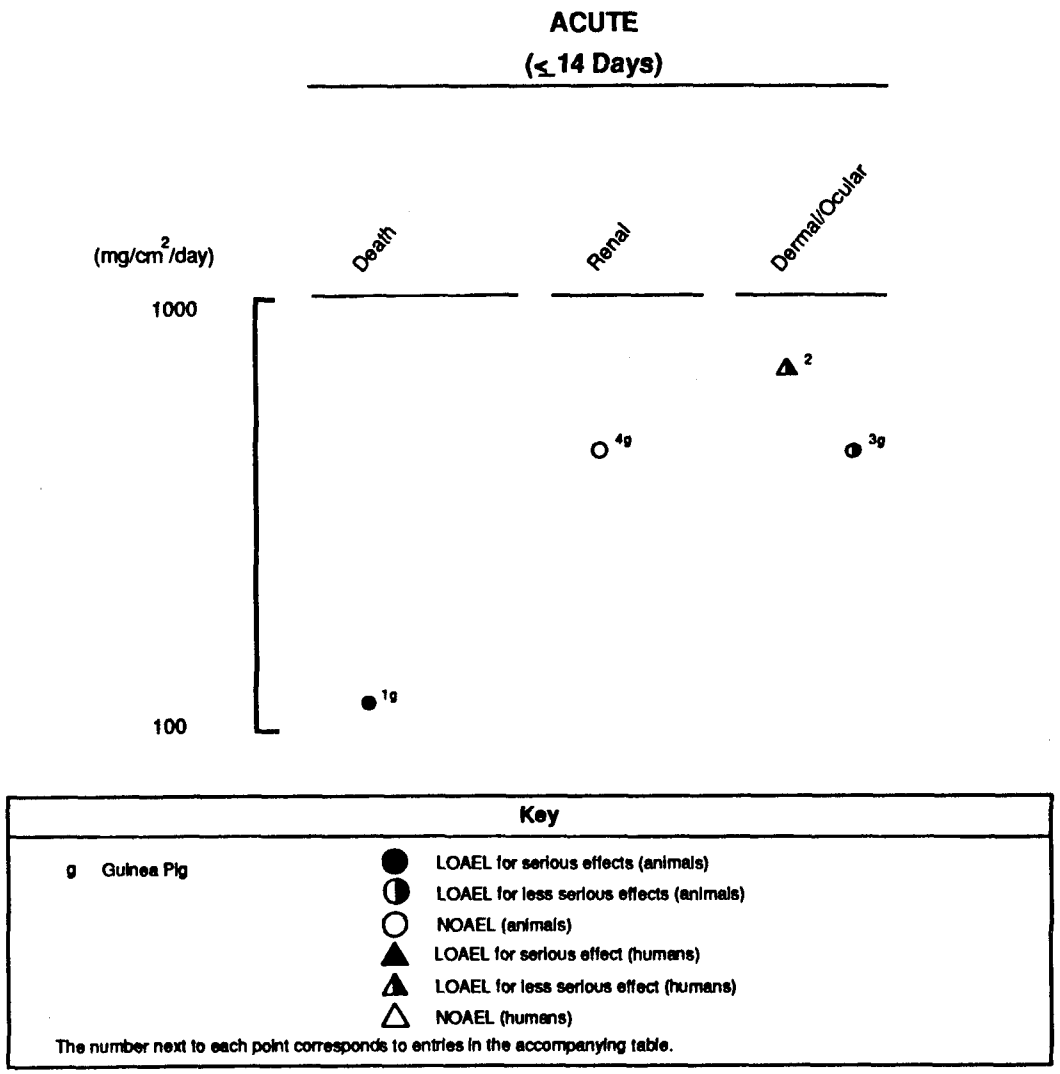


FIGURE 2-3. Levels of Significant Exposure to 1,1,2-Trichloroethane - Dermal

Renal Effects. No studies were located regarding renal effects in humans following dermal exposure to 1,1,2-trichloroethane.

The renal effects of dermally applied 1,1,2-trichloroethane in animals were examined in one study. No histopathological changes were found in the kidneys of guinea pigs 2, 6, or 12 hours after dermal application of 1,1,2-trichloroethane at 465 mg/cm^2 (Kronevi et al.mg/cm^{2}1977). The NOAEL of 465 is presented in Table 2-3 and plotted in Figure 2-3.

Dermal/Ocular Effects. The effect of 1,1,2-trichloroethane on the human skin was the subject of several reports. A human subject given 5 minute dermal exposure to 1,1,2-trichloroethane under occlusion at 698 mg/cm^2 (1.5 mL on 3.1 cm^2 of the forearm) reported stinging and burning sensations and displayed transient whitening of the skin (Wahlberg 1984a). A small, immediate increase in blood flow was measured by laser Doppler flowmetry, but no visible erythema was present. The acute human LOAEL was taken to be 698 mg/cm^2 on the basis of this report (see Table 2-3 and Figure 2-3). In general, use of a cover disk markedly enhances the percutaneous absorption and dermal irritant properties of volatile organic chemicals, which would usually evaporate from the skin's surface. In an open test on the same subject, in which 0.1 mL of 1,1,2-trichloroethane was applied to the skin without a cover disc, there was no effect on blood flow and no visible erythema was found (Wahlberg 1984a). A volunteer given daily open application of 0.1 mL of 1,1,2-trichloroethane for 15 days did not have any visible skin reactions, nor was there any increase in skin-fold thickness, which was measured using calipers (Wahlberg 1984b). These doses are presented in Table 2-3, but could not be converted to per-area units in the open tests because the area of application was not limited to the 3.1 cm^2 of the cover disc, so they are not plotted in Figure 2-3.

The dermal effects of 1,1,2-trichloroethane have also been studied in animals. Dermal application of 1,1,2-trichloroethane at 465 mg/cm^2 produced pyknotic nuclei in epidermal cells within 15 minutes in guinea pigs (Kronevi et al. 1977). As the duration of exposure increased, damage progressed to vesicle formation and separation of skin layers (Kronevi et al. 1977). A LOAEL of 465 mg/cm^2 for acute dermal effects in guinea pigs is reported in Table 2-3 and plotted in Figure 2-3. Rabbits given a single application of 0.01 mL of 1,1,2-trichloroethane had no effects other than slight capillary congestion (Smyth et al. 1969) (see Table 2-3). This study was not plotted on Figure 2-3 because the dose was not reported in per-area units. Duprat et al. (1976) compared the dermal irritancy of chlorinated aliphatic solvents in rabbits and determined that 1,1,2-trichloroethane was a severe skin irritant compared to other compounds in this group, producing serious erythema, serious edema, and necrosis. The results of this study were not used for a LOAEL because no dose was reported. In a repeated-dose study, daily open application of 0.1 mL for 10 days increased skin-fold thickness 170% in guinea pigs and 218% in rabbits (Wahlberg 1984b). All animals in this study displayed marked erythema and edema, and fissuring and scaling

were also seen. The LOAEL is presented in Table 2-3 but not in Figure 2-3 because the dose was not reported in per-area units.

1,1,2-Trichloroethane applied directly to the eye did not produce significant cornea1 necrosis in rabbits (Smyth et al. 1969). It was classified as a slight eye irritant by Duprat et al. (1976), who found moderate catarrhal conjunctivitis and epithelial abrasion following application in rabbits. Neither study reported the dose of 1,1,2-trichloroethane applied, so neither was used as the basis for a level of significant exposure.

2.2.3.3 Immunological Effects

No studies were located regarding immunological effects in humans or animals following dermal exposure to 1,1,2-trichloroethane.

2.2.3.4 Neurological Effects

No studies were located regarding neurological effects in humans following dermal exposure to 1,1,2-trichloroethane.

One study of neurological effects in animals was located. No histopathological changes were found in the brains of guinea pigs 2, 6, or 12 hours after dermal application of 1,1,2-trichloroethane at 465 mg/cm^2 (Kronevi et al. 1977). A NOAEL was not derived from this study because tests of nervous system function were not included, and histopathology alone may not be an adequate endpoint to assess neurotoxicity.

2.2.3.5 Developmental Effects

No studies were located regarding developmental effects in humans or animals following dermal exposure to 1,1,2-trichloroethane.

2.2.3.6 Reproductive Effects

No studies were located regarding reproductive effects in humans or animals following dermal exposure to 1,1,2-trichloroethane.

2.2.3.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans or animals following dermal exposure to 1,1,2-trichloroethane.

2.2.3.8 Cancer

No studies were located regarding cancer in humans or animals following dermal exposure to 1,1,2-trichloroethane.

2.3 RELEVANCE TO PUBLIC HEALTH

Other than studies on dermal irritation, no studies were located regarding health effects in humans following inhalation, oral, or dermal exposure to 1,1,2-trichloroethane; therefore, all implications for public health are derived from animal studies.

Lethality. 1,1,2-Trichloroethane produced mortality in animals by all routes of exposure tested, including inhalation, oral, dermal, intraperitoneal injection, and subcutaneous injection. Death was produced in rats, mice, guinea pigs, rabbits, and dogs, although not every species was tested by every route of exposure.

There is some evidence that mice were more susceptible than rats to 1,1,2-trichloroethane-induced mortality following acute inhalation, oral and intraperitoneal exposure. Inhalation LC_{50} values for rats and mice were 1654 and 416 ppm, respectively, in two studies done in the same laboratory (Bonnet et al. 1980, Gradiski et al. 1978). Oral LD_{50} values for rats and mice were 837 mg/kg (administered by gavage undiluted) and 378 mg/kg (administered by gavage as an aqueous emulsion), respectively, but only studies by different groups of investigators were available for comparison (Smyth et al. 1969, White et al. 1985). Rat and mouse intraperitoneal LD_{50} values were 938 and 505 mg/kg, respectively, in two tests performed by the same investigators (Klaassen and Plaa 1966, 1969). In each of these cases, mice proved to be more susceptible to death produced by 1,1,2-trichloroethane than rats. However, the maximum tolerated oral dose was higher in mice (300 mg/kg/day) than rats (70 mg/kg/day) in a 6-week study in which 1,1,2-trichloroethane was administered by gavage in corn oil (NCI 1978). Differences in duration of exposure, vehicle, and strain of animal used may account for the discrepancy between this study and the others. Metabolism of 1,1,2-trichloroethane occurs at a faster rate in mice than in rats (Mitoma et al. 1985), and it is possible that greater amounts of reactive metabolites in mice are responsible for the species difference in susceptibility to this chemical.

In addition, there may be sex differences in sensitivity to 1,1,2-trichloroethane. This compound was more toxic to male mice (LD_{50} = 378 mg/kg) than female mice (LD_{50} = 491 mg/kg) following acute oral administration (White et al. 1985). However, survival was reduced in female mice given chronic oral administration of 1,1,2-trichloroethane, but not in males (NCI 1978). No sex difference was noted in LD_{50} values determined after intraperitoneal administration in a different strain of mice (Klaassen and Plaa 1969).

Levels of 1,1,2-trichloroethane that produce mortality have been identified in a number of species, and by several routes of exposure. Exposure to high levels of 1,1,2-trichloroethane may also be fatal to humans. Species and sex variation in susceptibility make it difficult to estimate the level at which this compound might produce death in humans.

Hepatic Effects. 1,1,2-Trichloroethane had adverse effects on the livers of rats, mice, guinea pigs, and dogs when administered orally or by inhalation. These effects included necrosis, elevated SGPT and SGOT levels, and reduced liver glycogen content (Gehring 1968, Tyson et al. 1983, White et al. 1985, Wright and Schaffer 1932). Intraperitoneal studies in these same four species revealed similar hepatic effects, including centrilobular necrosis, elevated SGPT levels, increased serum ornithine carbamyl transferase activity, and fatty changes (Klaassen and Plaa 1966, Klaassen and Plaa 1967a, Traiger and Plaa 1974, Divincenzo and Krasavage 1974, Harms et al. 1976, MacDonald et al. 1982). 1,1,2-Trichloroethane was also toxic to isolated rat hepatocytes in vitro (Tyson et al. 1980, Jernigan et al. 1983, Chang et al. 1985). A sex difference in susceptibility was noted by White et al. (1985), who reported that female mice exposed to 384 mg/kg/day in the drinking water for 90 days had significantly elevated SGPT levels, but males exposed to 304 mg/kg/day did not. These investigators also found that liver glutathione decreased in males and increased in females. Although there is no information available to suggest that 1,1,2-trichloroethane is a liver toxin in humans, it is considered a potential human hepatotoxin because experiments in animals indicate hepatotoxic potential in all species tested.

One mechanism that has been proposed to explain the hepatotoxicity of 1,1,2-trichloroethane is the generation of free radical intermediates from reactive metabolites of 1,1,2-trichloroethane (acyl chlorides). Free radicals may stimulate lipid peroxidation which, in turn, may induce liver injury (Albano et al. 1985). However, Klaassen and Plaa (1969) found no evidence of lipid peroxidation in rats given near-lethal doses of 1,1,2-trichloroethane by intraperitoneal injection. Takano and Miyazaki (1982) determined that 1,1,2-trichloroethane inhibits intracellular respiration by blocking the electron transport system from reduced nicotinamide adenine dinucleotide (NADH) to coenzyme Q (CoQ), which would deprive the cell of energy required to phosphorylate adenosine diphosphate (ADP) and thereby lead to depletion of energy stores.

Renal Effects. There was only one reliable report of kidney damage following oral exposure to 1,1,2trichloroethane. Wright and Schaffer (1932) found cloudy swelling and congestion in the kidneys of treated dogs. No kidney pathology was found after dermal application in guinea pigs (Kronevi et al. 1977) or inhalation exposure in rats (Bonnet et al. 1980). One unpublished study reported kidney damage following inhalation exposure in rats [Dow Chemical Co. (cited in Torkelson and Rowe 1981)].

Renal effects in mice and dogs given intraperitoneal or subcutaneous injections of 1,1,2-trichloroethane were studied in a series of experiments by Plaa and co-workers. Although no gross effects were visible, tubular lesions with necrosis were seen microscopically in the cortex of the kidneys of mice injected subcutaneously with 173 mg/kg 1,1,2-trichloroethane (Plaa et al. 1958). The ED_{50} for necrosis, swelling of the kidney, and renal dysfunction in mice, as indicated by increased protein and glucose in the

urine, was 216 mg/kg by intraperitoneal injection (Plaa and Larson 1965). Klaassen and Plaa (1966, 1967a) found necrosis and reduced ability to excrete intravenously-administered PSP (phenolsulfonphthalein) in the kidneys of male mice and dogs given 1,1,2-trichloroethane intraperitoneally. Female mice did not show this effect, even at lethal doses (Klaassen and Plaa 1967b). This evidence strongly suggests a sex difference in susceptibility to the renal effects of 1,1,2-trichloroethane in mice, but the reason for this difference is not known.

There is good evidence that 1,1,2-trichloroethane is nephrotoxic when parenterally administered in mice and dogs. There is also some evidence for kidney effects in animals following inhalation and oral exposure. These results suggest that 1,1,2-trichloroethane may be nephrotoxic in humans.

Immunological Effects. A detailed study of the effects of 1,1,2-trichloroethane on the immune system was performed by Sanders et al. (1985). They reported that significant effects on mouse immune function were found at doses as low as 44 to 46 mg/kg/day in a 90-day study. Humoral immune function, functional activity of the fixed macrophages of the reticuloendothelial system, and macrophage phagocytic activity were all affected (although the latter two were only altered in high-dose mice). These data suggest that 1,1,2-trichloroethane may interfere with immune function in animals. It is possible that these effects could also be produced in humans exposed to 1,1,2-trichloroethane, although there are no data currently available indicating immune system effects in humans.

There was a distinct sex difference in immune response to 1,1,2-trichloroethane exposure in mice. Some effects, such as reduced spleen lymphocyte response to lipopolysaccharide and increased vascular clearance by the fixed macrophages of the reticuloendothelial system, were found only in females. Others, such as depressed ability to phagocytize sheep red blood cells, occurred only in males. The reason for these differences is not known and their significance for human health is unclear.

Neurological Effects. Anesthesia has been produced in animals by oral intake, inhalation, and intraperitoneal injection of 1,1,2-trichloroethane. This effect has been studied in both mice and dogs. The ED_{50} for motor impairment in mice reported by Borzelleca (1983) was approximately one third the LD_{50} value for mice reported by White et al. (1985). At an inhalation concentration of 3750 ppm, the ET_{50} (time required to produce anesthesia in one-half of the treated animals) was 18 minutes, which is much less than the LT_{50} of 10 hours in this study (Gehring 1968). The occurrence of anesthetic effects at doses well below those that produce death indicates that 1,1,2-trichloroethane is a potent CNS depressant.

Central nervous system depression was reported by De Ceaurriz et al. (1981) following inhalation exposure in mice. Tham et al. (1984) found that intravenous infusion of 28 mg/kg 1,1,2-trichloroethane had a depressive effect on the vestibulo-oculomotor reflex in rats. Taste aversion, which

represents a conditioned avoidance response, was another neurological effect produced by 1,1,2-trichloroethane. Kallman et al. (1983) suggest that taste aversion may be sensitive to the acute health effects of 1,1,2-trichloroethane, but that it may not be useful in assessing delayed or cumulative toxicity. No data on neurological effects of 1,1,2-trichloroethane in humans were located, but the evidence in animals suggests that this compound may have central nervous depressant effects in humans as well.

Genotoxic Effects. Data on the genotoxic effects of 1,1,2-trichloroethane are presented in Tables 2-4 and 2-5. In vitro mutagenicity assays were negative in Salmonella typhimurium and positive in Saccharomvces cerevisiae. A cell transformation assay performed in the absence of activation on mouse BALB/c-3T3 cells was negative. A test of DNA repair in cultured rat hepatocytes was positive, but one in mouse hepatocytes was not (Williams 1983). Adduct formation with calf thymus DNA occurred in vitro at a significant rate (DiRenzo et al. 1982a). DNA adduct formation in vivo occurred to a greater extent in mouse liver than in rat liver (Mazzullo et al. 1986). The authors point out that there is a correlation between these adduct formation results and species susceptibility to cancer, as the incidence of hepatocellular carcinomas was increased in mice, but not rats, given 1,1,2-trichloroethane for 78 weeks. Finally, DNA synthesis was inhibited by intratesticular injection of 1,1,2-trichloroethane in the mouse (Borzelleca 1983). Although there are negative as well as positive results, it is evident that this compound does have some genetic effects both in vitro and in vivo. The significance of these effects for humans is not clear, especially since results of in vivo mammalian assays showed species variability.

Cancer. There is no evidence for carcinogenicity of 1,1,2-trichloroethane in humans. Among animals, 1,1,2-trichloroethane was carcinogenic in $B6C3F_1$ mice, but not Osbourne-Mendel rats. In a gavage study by NCI (1978), this compound produced significant increases in the incidence of hepatocellular carcinomas and adrenal pheochromocytomas in mice. Based on this study, Gold et al. (1987) calculated the carcinogenic potency (TD50) of 1,1,2-trichloroethane in mice to be 47.6 mg/kg/day, which is similar to the value for chloroform and about one third the value for carbon tetrachloride. No increase in the incidence of neoplasms was observed in rats under the conditions of the NCI bioassay. Carcinogenicity in rats was also studied by Norpoth et al. (1988), who found that subcutaneous injection of 15.4 or 46.8 μmol of 1,1,2-trichloroethane in DMSO once a week for 2 years had no effect on the incidence of benign mesenchymal and epithelial tumors in Sprague-Dawley rats. The incidence of sarcomas (mostly localized on the extremities) increased with dose in both sexes and was significantly elevated in high-dose rats compared to untreated controls. However, the lack of any sarcomas in the untreated controls was unusual for this strain, and when compared to the spontaneous incidence of sarcomas reported in the literature, this effect was no longer significant. In addition, sarcoma incidence was not elevated when compared to vehicle controls. From the

TABLE 2-4. Genotoxicity of 1,1,2-Trichloroethane In Vitro

Endpoint	Species/Test System	Result (Activation) With	Result (Activation) Without	References
Gene mutation	Salmonella typhimurium	-	-	Simmon et al. 1977 Rannug et al. 1978 Barber and Donish 1982 Mitoma et al. 1984 Zeiger et al. 1988
Gene conversion	Saccharomyces cerevisiae	+	+	Bronzetti et al. 1987
Cell transformation	mouse BALB/c-3T3 cells	NT	-	Tu et al. 1985
DNA repair	mouse hepatocytes	NA	-	Williams 1983
	rat hepatocytes	NA	+	Williams 1983
DNA adduct formation	calf thymus	NA	+	DiRenzo et al. 1982

NT = Not tested
NA = Not applicable

Table 2-5. Genotoxicity of 1,1,2-Trichloroethane In Vivo

Endpoint	Species (Test System)	Result	Reference
DNA adduct formation	mouse liver	+	Mazzullo et al. 1986
	rat liver	+	Mazzullo et al. 1986
Inhibition of DNA synthesis	mouse testis	+	Borzelleca 1983

limited evidence in mice, 1,1,2-trichloroethane has been classified in Group C as "a possible carcinogen" (EPA 1988a).

The mechanism of 1,1,2-trichloroethane carcinogenicity in mice is not known. Metabolism of this compound involves formation of acyl chlorides and free radicals, which may play a role in cancer formation. Although 1,1,2-trichloroethane has not been shown to be carcinogenic in rats, a study of cancer initiation and promotion in this species was located. Story et al. (1986) gave a single oral dose of 1,1,2-trichloroethane at 69 mg/kg in corn oil to rats and followed this treatment with 8 weeks administration of phenobarbital, a promoter of hepatocellular carcinomas. Using liver foci with altered enzyme levels as pre-neoplastic markers, they found no evidence that 1,1,2-trichloroethane acted as an initiator. The reciprocal experiment, using diethylnitrosamine (DEN) as the initiator and 1,1,2-trichloroethane as the possible promoter, gave similar results whether or not DEN initiation was given. In either case, there was a large increase in the total number of liver foci. However, when examined more closely, it was found that these increases occurred solely in the number of Type II foci, which do not appear to be preneoplastic. Therefore, no evidence of cancer promotion by 1,1,2-trichloroethane was found in this study.

2.4 LEVELS IN HUMAN TISSUES AND FLUIDS ASSOCIATED WITH HEALTH EFFECTS

No studies were located regarding the levels of 1,1,2-trichloroethane in human tissues and fluids associated with effects.

2.5 LEVELS IN THE ENVIRONMENT ASSOCIATED WITH LEVELS IN HUMAN TISSUES AND/OR HEALTH EFFECTS

The levels of 1,1,2-trichloroethane were studied in 230 personal air samples, 170 drinking water samples, 66 breath samples and 16 food samples from 9 volunteers in New Jersey and 3 in North Carolina (Wallace et al. 1984). In 99% of the cases, no 1,1,2-trichloroethane or only trace amounts were found in the environment, or in the exhaled breath of the people. Specifically, the personal air concentrations of 1,1,2-trichloroethane were below the detection limit in 151/161 samples, 7 contained trace levels, and the others had a very low median value of 0.35 $\mu g/m^3$ (0.063 ppb). Breath samples were negative in 44/49 samples, value of 0.2 $\mu g/m^3$ (0.036 ppb). and the others had a very low median

The levels of halogenated organic compounds were studied in the Ruhr region of West Germany from 1976-1978 (Bauer 1981a,b). The concentration of 1,1,2-trichloroethane in the Rhine river at this time averaged 0.2 $\mu g/L$ (ppb), and the concentration in the drinking water in 100 German cities had a maximum of 5.8 $\mu g/L$ (ppb). Air concentrations rarely were over 1 $\mu g/m^3$ (0.18 ppb) and 1,1,2-trichloroethane was not detected in the foods or cosmetic products available locally. The average concentrations in humans tissues studied in 15 people who were exposed primarily via the air (94% of the exposure) were 6 $\mu g/kg$ in adrenal capsule adipose tissue, 14 $\mu g/kg$ in

subdermal adipose tissue, 2 μg/kg in the lungs, 3 μg/kg in the liver, and 17 μg/kg in the muscle tissue. This study does not establish levels in human tissue associated with health effects.

2.6 TOXICOKINETICS

2.6.1 Absorption

2.6.1.1 Inhalation Exposure

Studies in humans indicate that 1,1,2-trichloroethane is absorbed rapidly after inhalation exposure (Morgan et al, 1970, 1972). A volunteer took one breath of radiolabeled 1,1,2-trichloroethane and expired 10% of the inspired dose in the alveolar air after 12 seconds and about 0.5% after 40 seconds of breath-holding. More than 90% of the administered dose was retained in the body after 50 minutes. These data indicate that 1,1,2-trichloroethane was extensively absorbed into the bloodstream.

The only data on absorption of 1,1,2-trichloroethane following inhalation exposure in animals comes from the assumption that an administered chemical has been absorbed by the body if it can be shown to affect physiological processes. 1,1,2-Trichloroethane has been shown to affect the exhalation of acetone in rats (Filser et al. 1982), so it can be assumed that the 1,1,2-trichloroethane was absorbed.

2.6.1.2 Oral Exposure

No studies were located regarding absorption in humans following oral exposure to 1,1,2-trichloroethane. The only data available in animals showed that oral doses near the MTD (maximum tolerated dose) in mice (300 mg/kg) or rats (70 mg/kg) were 81% metabolized, indicating that at least this amount was absorbed (Mitoma et al. 1985). This suggests that 1,1,2-trichloroethane, like other structurally related halocarbons, is well absorbed from the gastrointestinal tract of animals, and probably humans as well.

2.6.1.3 Dermal Exposure

No studies were located regarding absorption in humans following dermal exposure to 1,1,2-trichloroethane. Two studies in animals indicate that 1,1,2-trichloroethane is easily absorbed through the skin. In the guinea pig, blood concentration of 1,1,2-trichloroethane peaked at ≈3.7 μg/mL within a half-hour following 1,1,2-trichloroethane application to the skin (Jakobson et al. 1977). Following the peak, the blood level declined to ≅2.5 μg/L at 1 hour, remained at this level until ≅4 hours, and then rose to ≅3.7 μg/L at 6 hours. The authors suggested that this complex dermal absorption of 1,1,2-trichloroethane may be due to an initial increased barrier function of the skin after 1. hour, which led to decreased absorption. Subsequent absorption during the next few hours may represent

an overcoming of the barrier. In mice, 15 minutes after application of 0.5 ml of 1,1,2-trichloroethane, 99.7% was retained in the body and 0.3% was expired in the breath (Tsuruta 1975). The absorption rate was calculated to be 130 nmoles/min/cm^2 of skin. The rapid absorption through the skin may well be due to the highly lipid soluble character of 1,1,2-trichloroethane (Kronevi et al. 1977).

2.6.2 Distribution

2.6.2.1 Inhalation Exposure

No studies were located regarding distribution in humans following inhalation of 1,1,2-trichloroethane. After an inhalation exposure of 1000 ppm for 1 hour, 1,1,2-trichloroethane was distributed in mice organs in the following manner: approximately 600 μg/g in fats, 80 μg/g in the kidney and liver, 45-60 μg/g in the blood and brain, and 20-35 μg/g in the heart, spleen and lung (Takahara 1986a). Examination of partition coefficients showed that 1,1,2-trichloroethane had a moderate degree of lipid solubility compared to other hydrocarbons, but was still quite lipid soluble (Gargas et al. 1989, Imbriani et al. 1985, Morgan et al. 1972, Sato and Nakajima 1979). This indicates that 1,1,2-trichloroethane could be easily distributed and retained in fat, liver, and brain in both animals and humans.

2.6.2.2 Oral Exposure

No studies were located regarding distribution in humans or animals following oral exposure to 1,1,2-trichloroethane. One study showed that 1,1,2-trichloroethane was distributed to the liver following oral exposure in animals (Mitoma et al. 1985). In this study, 1,1,2-trichloroethane was extensively metabolized (presumably by the liver), and was also found to bind hepatic protein. It is likely that 1,1,2-trichloroethane is also distributed to the liver in humans.

2.6.2.3 Dermal Exposure

No studies were located regarding distribution in humans or animals following dermal exposure to 1,1,2-trichloroethane.

2.6.3 Metabolism

No studies were located regarding metabolism in humans following exposure to 1,1,2-trichloroethane.

The primary metabolites identified by high-performance liquid chromatography in rats and mice given 1,1,2-trichloroethane by gavage were chloroacetic acid, S-carboxymethylcysteine, and thiodiacetic acid (Mitoma et al. 1985). An earlier study reported these three compounds to be the primary metabolites of 1,1,2-trichloroethane following intraperitneal injection (Yllner 1971). S-carboxymethycysteine and thiodiacetic acid are

formed from 1,1,2-trichloroethane following conjugation with glutathione (Yllner 1971). Chloroacetic acid is formed by hepatic cytochrome P-450 (Ivanetich and Van Den Honert 1981). This reaction is thought to proceed via the acyl chloride. Cytochrome P-450 can also produce free radicals from 1,1,2-trichloroethane (Mazzullo et al. 1986). These proposed pathways are shown in Figure 2-4. Acyl chlorides and free radicals are reactive metabolites that can bind to proteins and nucleic acids, and are suspected of being cytotoxic, mutagenic, and carginogenic (Ivanetich and Van Den Honert 1981, Mazzullo et al. 1986). Other metabolites, found only in trace amounts in mice and rats following exposure to 1,1,2-trichloroethane, included trichloroacetic acid and trichloroethanol (Ikeda and Ohtsuji 1972, Takahara 1986b, Yllner 1971). It is not clear how these compounds were formed; it was suggested by Yllner (1971) that they might be derived from impurities in the 1,1,2-trichloroethane samples used.

Although percent of the orally-administered dose metabolized was identical in rats and mice (81%), the actual amount of 1,1,2-trichloroethane metabolized was much higher in mice (Mitoma et al. 1985). The chemical was given to each species at the MTD, which was 4.3 times greater in mice; mice experienced a higher body burden than rats, but were able to metabolize the same percentage of it. The inherent ability of mice to metabolize 1,1,2-trichloroethane at a higher rate than rats may contribute to the greater susceptibility of mice to 1,1,2-trichloroethance cytotoxicity and carcinogenity. It is not known how the rate of 1,1,2-trichloroethane metabolism *in* humans compares to that in mice and rats. Metabolism in humans is likely to be qualitatively similar to that in animals, however.

2.6.4 Excretion

2.6.4.1 Inhalation Exposure

The excretion rate of inhaled 1,1,2-trichloroethane in humans was measured in the breath and urine of humans (Morgan et al. 1970). Excretion in the breath after 1 hour was 2.9% of the administered dose; the slope of the retention curve was 0.006. The excretion rate in the urine was less than 0.0l%/min of administered radioactivity. From these data, the half-life for urinary excretion was estimated to be about 70 minutes.

The half-life following l-hour inhalation exposure to 1005 ppm of 1,1,2-trichloroethane in mice was determined to be 625 minutes in the heart, 203 minutes in the fat, 147 minutes in the brain, 127 minutes in the spleen, 122 minutes in the lungs, 43 minutes in the kidney, 39 minutes in the blood, and 19 minutes in the liver (Takahara 1986a). The half-life in the whole body was calculated to be 49.3 minutes. The presence of 1,1,2-trichloroethane in tissue samples was determined by gas chromatography,

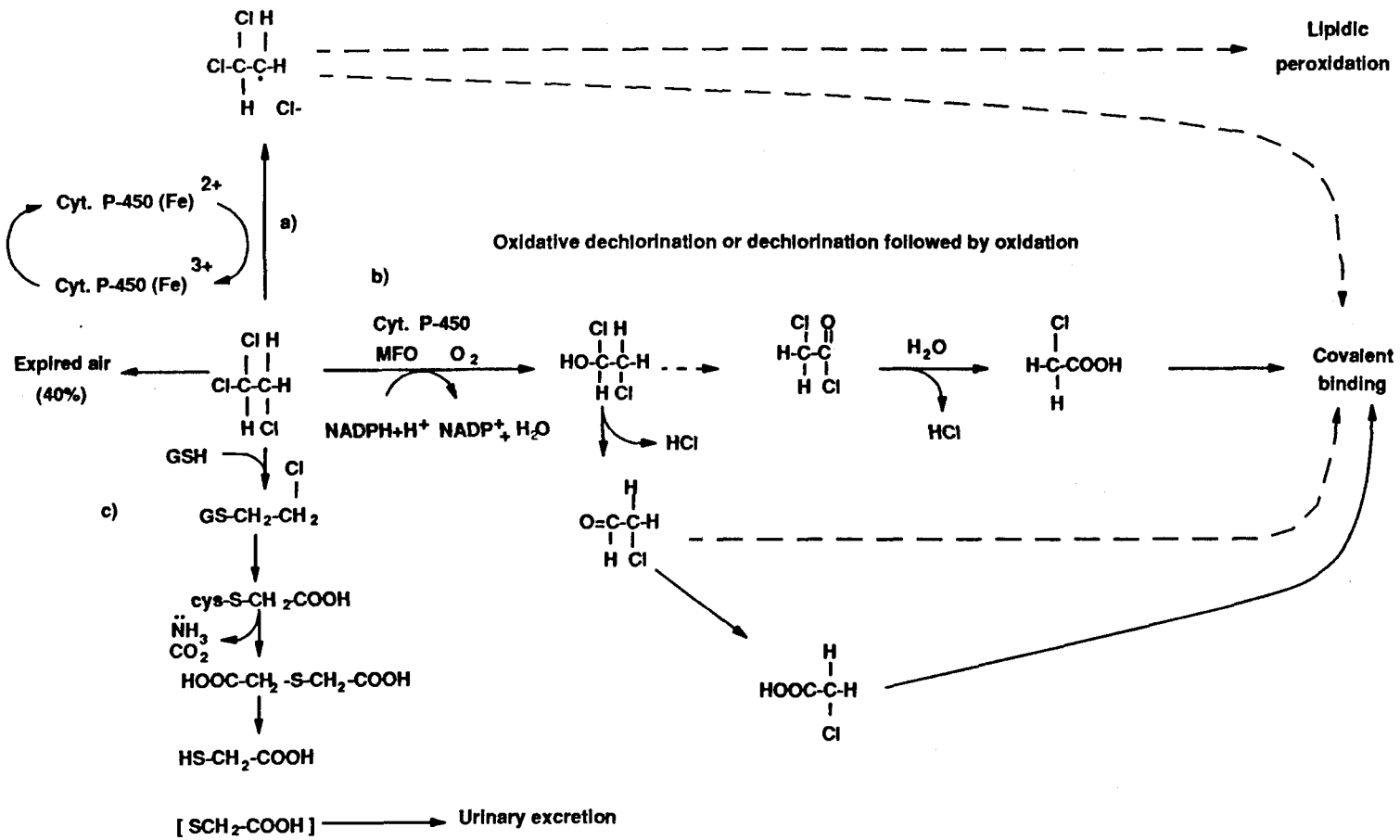


FIGURE 2-4. Proposed Metabolic Pathway of 1,1,2-Trichloroethane. a) one-electron oxidation; b) two-electron oxidation; c) detoxification step. - - - supposed pathway; —proven pathway.

(from Mazzullo et al. 1986)

2.6.4.2 Oral Exposure

No studies were located regarding excretion in humans following oral exposure to 1,1,2-trichloroethane.

The excretion routes were shown to be similar in rats and mice, regardless of whether the chemical was given orally (Mitoma et al. 1985) or intraperitoneally (Yllner et al. 1971). Following a dose of radiolabeled compound, about 7-10% of 1,1,2-trichloroethane was exhaled unchanged in the breath, 3-7% was exhaled as $C0_2$, 72%-87% was found as metabolites in the urine, about 1% was in the feces, and l-3% remained in the carcasses of rats and mice after 48 hours. The excretion from humans is also likely to be primarily via metabolites in the urine.

2.6.4.3 Dermal Exposure

No studies were located regarding excretion in humans or animals following dermal exposure to 1,1,2-trichloroethane.

2.7 INTERACTIONS WITH OTHER CHEMICALS

Polybrominated biphenyls (PBBs) were shown to increase the renal toxicity of 1,1,2-trichloroethane as measured by decreases in paminohippurate accumulation in renal cortical slices (Kluwe et al. 1978). PBBs are known to increase the activities of microsomal mixed-function oxygenases in the kidney and liver, so increased metabolism of 1,1,2-trichloroethane and the increased presence of metabolites more toxic than the parent compound itself may be responsible for the increased toxicity of 1,1,2-trichloroethane in the kidney. However, the study also showed that PBBs did not increase the hepatotoxic effects of 1,1,2-trichloroethane, as indicated by relative liver weight or SGOT levels.

Phenobarbital, another microsomal enzyme inducing agent, was found to potentiate liver toxicity, as indicated by increases in SGOT and SGPT in rats that were exposed to 1,1,2-trichloroethane vapor (Carlson 1973). Guinea pigs treated with pentobarbital as an anesthetic following dermal application of 1,1,2-trichloroethane were shown to have reduced glycogen levels and hydropic changes in the liver (Kronevi et al. 1977). Liver effects were not found in anesthetized "control" animals or animals that were treated with 1,1,2-trichloroethane, but not anesthetized. The authors suggest that the liver effects they observed were produced by the interaction of pentobarbital and 1,1,2-trichloroethane. The lack of untreated controls makes this claim difficult to evaluate, however. Potentiation is usually seen only after pretreatment with the inducer, since time is required for enzyme induction. It may be that dermal absorption of 1,1,2-trichloroethane was slow enough, compared to intraperitoneal absorption of pentobarbital, for this to occur.

Pretreatment with low, but not high doses of acetone (MacDonald et al. 1982) potentiated the hepatotoxicity of 1,1,2-trichloroethane in rats as indicated by a rise in SGPT and a decrease in hepatic GSH levels. Acetone also potentiated the 1,1,2-trichloroethane-induced elevation of SGPT in mice (Traiger and Plaa 1974).

Pretreatment with isopropyl alcohol (Traiger and Plaa 1974) or ethanol (Klaassen and Plaa 1966) potentiated the 1,1,2-trichloroethane-induced elevation of SGPT activity in mice. Pretreatment with ethanol did not alter BSP retention (Klaassen and Plaa 1966).

Pretreatment with alloxan, which induces a hyperglycemic state similar to that found in diabetic humans, also enhanced the hepatotoxic effects of 1,1,2-trichloroethane in rats as indicated by increased SGPT activity and increased hepatic triglyceride concentration (Hanasono et al. 1975). The mechanism of this interaction is unknown.

2.8 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

Persons with diabetes (Hanasono et al. 1975), or with prior exposure to PBBs (polybrominated biphenyls) (Kluwe et al. 1978), or with prior exposure to isopropyl or ethyl alcohol or acetone (Traiger and Plaa 1974) may be more susceptible to the hepatotoxic effects of 1,1,2-trichloroethane. Prior exposure to other enzyme-inducing drugs or chemicals could potentially have the same effect.

2.9 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of DCE is available. Where adequate information is not available, ATSDR, in cooperation with the National Toxicology Program (NTP), is required to assure the initiation of a program of research designed to determine these health effects (and techniques for developing methods to determine such health effects). The following discussion highlights the availability, or absence, of exposure and toxicity information applicable to human health assessment. A statement of the relevance of identified data needs is also included. In a separate effort, ATSDR, in collaboration with NTP and EPA, will prioritize data needs across chemicals that have been profiled.

2.9.1 Existing Information on Health Effects of Trichloroethane

Existing studies on the health effects of 1,1,2-trichloroethane are shown in Figure 2-5. Almost no data exist for the health effects of this compound in humans; a single study on the dermal irritation of 1,1,2-trichloroethane in man was located in the literature.

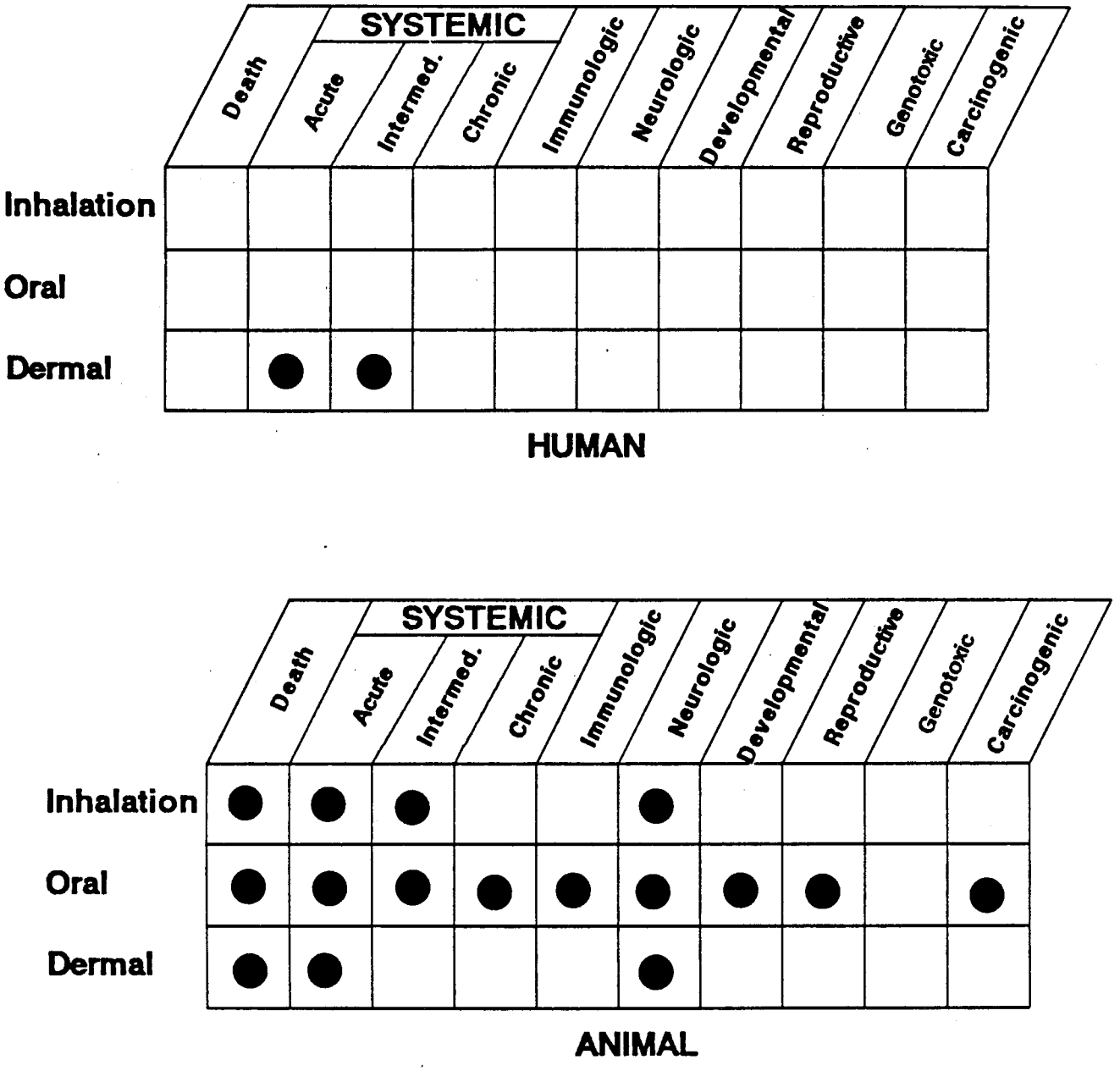


FIGURE 2-5. Existing Information on the Health Effects of 1,1,2-Trichloroethane

The health effects of 1,1,2-trichloroethane in animals have been fairly well studied. A number of inhalation studies investigated lethality in rats and mice, and several made LC_{50} determinations. The systemic effects that have been studied following inhalation exposure are liver and kidney effects. Liver effects were investigated in several studies that measured serum transaminase levels and other biochemical endpoints; only one unpublished study included histopathological examination of the liver. The same study included histopathological examination of the kidney. This study was also the only one in which animals were repeatedly exposed to 1,1,2-trichloroethane vapor; all other studies by this route were single exposure tests. Neurological effects following inhalation were studied by behavioral observations in rats and mice and tests of neurological function in mice.

Following oral exposure, lethality in rats, mice, and dogs has been reported. LD_{50} values were calculated for the first two species. Systemic effects were studied in rats, mice, and dogs using biochemical and histopathological measures. Most studies were of single exposures, but there was one study of intermediate duration (which did not include histopathological examination) and one of chronic duration (which included only histopathologic examination). Immunological effects were reported in a study that included tests of humoral and cell-mediated immune function. Neurological effects were studied by behavioral observation and, in longerterm studies, examination of tissues. Developmental toxicity was the subject of one study that did not include examination of fetuses for malformations. Data on reproductive effects come from this study and longer-term studies that examined reproductive tissues, but did not perform tests of reproductive function. Carcinogenicity was studied in one 78-week bioassay in rats and mice and one 2-year study in rats that was not, however, performed by a relevant route of exposure.

There is one study of lethality in guinea pigs following dermal exposure to 1,1,2-trichloroethane. There are also several studies of skin and eye irritation in dermally-exposed animals. One poorly-designed study investigated the effect of dermally applied 1,1,2-trichloroethane on liver, kidney, and brian histopathology.

2.9.2 Data Needs

Single Dose Exposure. Tests of the acute toxicity of 1,1,2-trichloroethane administered orally and by inhalation have provided information on 1,1,2-trichloroethane exposure levels that produce liver and kidney damage, neurological effects, and death in animals. Several of these studies included analyses for subtle liver effects, but few included histopathological examinations. More studies which carefully examine liver and other tissues histologically and look for subtle effects on other organs may be beneficial. They might provide information on mechanisms by which 1,1,2-trichloroethane produces lethality and neurological effects and provide further information on other toxic effects. Knowledge of mechanisms

is helpful to understanding the health effects of a chemical. Dermal studies of 1,1,2-trichloroethane have provided information on exposure levels that produce skin irritation in humans and animals and death in animals. One poorly-designed study attempted to investigate systemic effects in dermally exposed animals. A study of systemic toxicity following dermal application of 1,1,2-trichloroethane might provide useful information.

Repeated Dose Exposure. Only one study examined the health effects of 14- and 90-day ingestion of 1,1,2-trichloroethane in drinking water of animals, and it did not include histopathological examinations. A subchronic oral study with complete histological examination would be useful. Repeated dose exposure by inhalation was examined only in an unpublished report that could not be obtained for review. A published report of this study or a replacement would provide useful information. Repeated dermal application of 1,1,2-trichloroethane to humans was done in one study. No effects were found, but the irritancy of 1,1,2-trichloroethane in single-dose exposure tests suggests that repeated-exposure dermal tests in animals would provide meaningful information.

Chronic Exposure and Carcinogenicity. A 78-week bioassay on orally administered 1,1,2-trichloroethane was performed in rats and mice by the National Cancer Institute. 1,1,2-Trichloroethane was found to be cancerous in mice, but not rats. The 78-week dosing period is no longer considered adequate for rats. Current studies of this type use exposure durations of approximately 2 years. A 2-year study was conducted by Norpoth et al. (1988), but exposure was by subcutaneous injection, which is not a relevant route. Two-year studies by the oral and inhalation routes on rats and mice using several doses, examining endpoints of hematology, clinical chemistry, urinalysis, and performing microscopic examination of tissues may provide valuable dose-response data and identify more subtle indicators of toxicity. Studies of chronic toxicity and carcinogenicity do not exist for other routes of exposure.

Genotoxicity. The available genotoxicity studies indicate that *1,1,2*-trichloroethane is not mutagenic in bacteria, but may interact with mammalian DNA in vivo. Chromosomal aberration and micronucleus tests on 1,1,2-trichloroethane were not located. Additional genotoxicity tests would help to determine whether 1,1,2-trichloroethane is genotoxic in humans.

Reproductive Toxicity. Several studies included examination of reproductive organs and tissues following exposure to 1,1,2-trichloroethane, but found no effects. One study designed to look at developmental toxicity reported no effect on reproductive endpoints. Studies in which animals exposed to 1,1,2-trichloroethane are mated and their offspring observed would provide more information regarding the reproductive toxicity of 1,1,2-trichloroethane.

Developmental Toxicity. A study on the developmental toxicity of 1,1,2-trichloroethane in mice found no effect, but it did not include examination of the fetuses for malformations. A complete teratology study in two species would provide better information on the developmental toxicity of 1,1,2-trichloroethane in animals and help to determine whether it is possible that 1,1,2-trichloroethane has developmental effects in humans.

Immunotoxicity. The immunological effects of 1,1,2-trichloroethane have been studied following 14-day and 90-day oral exposure. Several measures of both humoral and cell-mediated immune response were investigated in this study, and some positive results were found. The fact that effects were found in some tests, but not others intended to measure the same response, indicates that more studies of this type could provide worthwhile information. In addition, immune responses were different in male and female mice, and investigation of these differences might provide meaningful information. No studies were located regarding dermal sensitization by 1,1,2-trichloroethane.

Neurotoxicity. Studies of 1,1,2-trichloroethane in animals have provided information on the neurological effects produced by acute exposure to 1,1,2-trichloroethane, and the levels at which they occur. The results of one study suggested that taste aversion may be a sensitive indicator of the acute neurological effects of 1,1,2trichloroethane. Additional neurobehavioral tests may reveal still more sensitive neurologic endpoints or provide support for use of taste aversion as an indicator of neurologic effects. Repeated exposure studies involved examination of neurological organs and tissues, but no tests of neurological function. Reliable studies of neurotoxicity by dermal exposure do not exist.

Epidemiological and Human Dosimetry Studies. No human studies were found in the literature which relate exposure to 1,1,2-trichloroethane with health effects. The evidence in animals, however, indicates that 1,1,2-trichloroethane can have effects on the nervous system, immune system, and liver and kidney function, and can be lethal. It is also carcinogenic in mice. These effects may also occur in humans, if they are exposed to appropriate levels of 1,1,2-trichloroethane. Epidemiological and human dosimetry studies might reveal whether humans are indeed susceptible to adverse health effects due to exposure to 1,1,2-trichloroethane.

Biomarkers of Disease. No studies were located that identified biomarkers specific for 1,1,2-trichloroethane-induced disease states. If epidemiological studies are performed that associate effects with exposure, it may be possible to identify alterations in blood chemistry indices or other pathological endpoints that would be useful to identify the disease state. Biomarkers for diagnosis of target organ toxicity (e.g., SGOT for liver damage) can provide useful information in conjunction with specific knowledge of 1,1,2-trichloroethane exposure,

Disease Registries. Currently, no human disease states are associated with exposure to 1,1,2-trichloroethane. If future studies identify particular diseases produced by 1,1,2-trichloroethane, it may be possible to determine the number of people affected and the factors associated with the development of the disease, such as involvement of populations in certain occupations or living in certain areas.

Bioavailability from Environmental Media. Since 1,1,2-trichloroethane is expected to exist in the atmosphere as the vapor rather than adsorb toparticulate matter, there would not be a competing adsorption that would impede its bioavailability via the lungs. Limited data showing the presence of 1,1,2-trichloroethane in adipose and other tissue of exposed subjects indicate that 1,1,2-trichloroethane is taken up via the lungs, GI tract or both. A pilot study demonstrated that similar low molecular weight chlorinated alkanes are found in human milk (Pellizzari et al. 1982). The source of these pollutants was probably ambient air, and this is the most probable route of intake for the general population.

Food Chain Bioaccumulation. 1,1,2-Trichloroethane has not been reported in food or biota, nor were any studies located in which the levels of this chemical in plants or animals were reported. The bioaccumulation potential for a chemical is most conveniently studied by measuring the bioconcentration factor (BCF) or the concentration of a chemical in fish divided by the concentration in water from which the chemical is taken up. The BCF of 1,1,2-trichloroethane in fish is reported to be <10 (Kawasaki 1980), indicating a very low potential for bioaccumulation in the food chain. Experimental verification of the lack of food chain bioaccumulation is not available. Such information can be obtained by studying the accumulation of 1,1,2-trichloroethane in organisms from different trophic levels that have been exposed to the chemical.

Absorption, Distribution, Metabolism, Excretion. Little information is available regarding the toxicokinetics of 1,1,2-trichloroethane in humans or animals. Information on absorption in humans comes from a brief study using two volunteers; the only information from animals is inferred from the fact that administration of 1,1,2-trichloroethane via the inhalation or oral routes causes toxic effects. Animal studies which specifically test the amount and rate of absorption of 1,1,2-trichloroethane would provide information as to how much 1,1,2-trichloroethane humans might be likely to absorb from various routes of exposure. For distribution, the only human data are from one briefly reported study, and the only animal data are from one acute study. More extensive and longer-term animal studies using the inhalation, oral or dermal routes would help determine 1,1,2-trichloroethane distribution in the body. For metabolism, more animal studies would be helpful in, showing what kind of metabolites might be expected to be found in the blood or urine of humans; if these could be measured, they might give an indication of amount of exposure to 1,1,2-trichloroethane. Additional metabolism studies may also reveal more

definitive information on mechanfsms of 1,1,2-trichloroethane toxicity and carcinogenicity. Data on excretion are fairly complete.

Comparative Toxicokinetics. No studies were located which compared human and animal toxicokinetics. Two comparative toxicokinetics studies were performed which examined the differences between rats and mice in the types of metabolites formed, and the excretion rates from various routes. Although percent of administered dose metabolized was similar in both species, the overall rate of metabolism of 1,1,2-trichloroethane was greater in mice (Mitoma et al. 1985). The same metabolites were formed in the same proportions in both species. The difference in metabolic rate may be related to species differences in susceptibility to the toxic effects of 1,1,2-trichloroethane. More studies of this type could corroborate this theory or identify other factors that may be responsible for the species difference in toxicity.

2.9.3 On-going Studies

No on-going studies were located regarding health effects or toxicokinetics in humans or animals following exposure to 1,1,2-trichloroethane.

3. CHEMICAL AND PHYSICAL INFORMATION

3.1 CHEMICAL IDENTITY

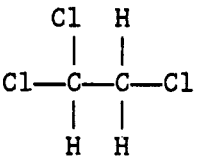
Data pertaining to the chemical identity of 1,1,2-trichloroethane are listed in Table 3-1,

3.2 PHYSICAL AND CHEMICAL PROPERTIES

The physical and chemical properties of 1,1,2-trichloroethane are presented in Table 3-2.

3. CHEMICAL AND PHYSICAL INFORMATION

TABLE 3-1. Chemical Identity of 1,1,1-Trichloroethane

	Value	Reference
Chemical Name	1,1,2-Trichloroethane	CAS 1988
Synonyms	Ethane trichloride; β-Trichloroethane; Vinyl trichloride; 1,2,2-Trichloroethane	CAS 1988; SANSS 1988
Trade Name(s)	β-T; Cement T-339	SANSS 1988
Chemical Formula	$C_2H_3Cl_3$	CAS 1988
Chemical Structure		
Identification Numbers:		
CAS Registry	79-00-5	CAS 1988
NIOSH RTECS	KJ2975000	NLM 1988
EPA Hazardous Waste	U227	NLM 1988
OHM/TADS	8100016	OHMTADS 1988
DOT/UN/NA/IMCO Shipping	None	
HSDB	1412	NLM 1988
NCI	CO4579	RTECS 1988

CAS = Chemical Abstracts Services
NIOSH = National Institute for Occupational Safety and Health
RTECS = Registry of Toxic Effects of Chemical Substances
OHM/TADS = Oil and Hazardous Materials/Technical Assistance Data System
DOT/UN/NA/IMCO = Department of Transportation/United Nations/North America/ International Maritime Dangerous Goods Code
NLMS = National Library of Medicine
HSDB = Hazardous Substance Data Bank
NCI = National Cancer Institute
SANSS = Structure and Nomenclature Search System

TABLE 3-2. *Physical and Chemical Properties of 1,1,2-Trichloroethane*

Property	Value	Reference
Molecular weight	133.41	Riddick et al. 1986
Color	Colorless	Hawley 1981
Physical state	Liquid	Hawley 1981
Freezing point	-36.53°C	Riddick et al. 1986
Boiling point	113.85°C	Riddick et al. 1986
Density, 20°C 20°C 20°C	1.43931 1.4416 1.443	Riddick et al. 1986 Merck 1983 Torkelson and Rowe 1981
Odor	Sweet	Hawley 1981
Odor threshold Water Air		
Solubility Water	4400 mg/L (20°C)	Riddick et al. 1986
Organic solvents	Miscible with ethers, alcohols, esters, and ketones	Hawley 1981
Partition coefficients Log octanol/water	2.42	Isnard and Lambert 1988
Log Koc	1.06-2.49[a] (estimated)	Sabljic 1987
Vapor pressure	22.49 mm Hg (25°C)	Riddick et al. 1986
Henry's Law constant	9.1×10^{-4} atm/m^3-mol (25°C); 1.12×10^{-3} atm/m^3-mol (30°C)[b]	Ashworth et al. 1988
Autoignition temperature	460°C	Parrish 1983

TABLE 3-2 (continued)

Property	Value	Reference
Flash point	None	Hawley 1981
Flammability limits	8.4-13.3% (by volume)	Moolenaar and Olson 1989
Conversion factors		
ppm (v/v) to mg/m^3 in air (20°C)	1 ppm (v/v) = 5.55 = mg/m^3	
mg/m^3 to ppm (v/v) in air (20°C)	1 mg/m^3 = 0.18 ppm (v/v)	

[a]Organic matter partition function.
[b]First value obtained using equilibrium partitioning in closed systems technique and second by the batch air-stripping method.

4 . PRODUCTION, IMPORT, USE, AND DISPOSAL

4.1 PRODUCTION

1,1,2-Trichloroethane is produced by Dow Chemical U.S.A. in Freeport, TX and by Olin Corporation in Seward, IL (SRI 1988). No production figures are available. It is produced in the U.S. from ethylene. In one method of preparation, ethylene is chlorinated to give 1,2-dichloroethane, which is then reacted with chlorine to give 1,1,2-trichloroethane (Archer 1979). A second method is via the oxychlorination of ethylene with hydrogen chloride and oxygen at 280-37°C in the presence of a catalyst (Archer 1979). 1,2-Dichloroethane and higher chlorinated ethanes are also formed in this process. 1,1,2-Trichloroethane is also produced as a coproduct in the thermal chlorination of l,l-dichloroethane to produce l,l,l-trichloroethane, especially when the reaction is carried out in the liquid phase (Archer 1979).

The only information pertaining to the amount of 1,1,2-trichloroethane produced dates back to 1979, when it was estimated that approximately 412 million pounds were produced (Thomas et al. 1982). This figure is the quantity of 1,1,2-trichloroethane required for maximum potential production of l,l-dichloroethene (vinylidene chloride) and may be an overestimate because l,l-dichloroethene can also be produced from l,l,l-trichloroethane (Thomas et al. 1982). The exact quantity manufactured is proprietary information of Dow Chemical Corporation, who was the sole producer of 1,1,2-trichloroethane at that time. Most of the chemical was captively consumed as a precursor for 1,1-dichloroethene, however according to a spokesperson from Dow a quantitity said to be in the 'low millions of pounds' is used annually in other industries (Thomas et al. 1982). It is not known whether the consumption of 1,1,2-trichloroethane has changed appreciably since 1979.

1,1,2-Trichloroethane is sometimes present as an impurity in commercial samples of l,l,l-trichloroethane and trichloroethylene (Henschler et al. 1980; Tsuruta et al. 1983). 1,1,2-Trichloroethane has been shown to be formed during the anaerobic biodegradation of 1,1,2,2-tetrachloroethane; anaerobic conditions may occur in groundwater or in landfills (Bouwer and McCarty 1983; Hallen et al. 1986).

4.2 IMPORT

Data pertaining to the import of 1,1,2-trichloroethane were not located in the available literature.

4.3 USE

The principal use of 1,1,2-trichloroethane is as a chemical intermediate in the production of l,l-dichloroethene (Archer 1979). There is no information available on the uses of the 'low millions of pounds' that were said to have been sold to other industries by Dow Chemical.

1,1,2-Trichloroethane finds limited use as a solvent where its high solvency is needed, such as for chlorinated rubbers (Archer 1979). It may be used as a solvent for fats, oils, waxes, and resins (Hawley 1981). Some 1,1,2-trichloroethane was sold for use in consumer products (Thomas et al. 1982). There was no indication in the literature as to what these products were. Moolenaar and Olson (1989), in a written communication as spokesmen for the Dow Chemical Company, a major producer of 1,1,2-trichloroethane, however, stated that they are not aware of any consumer uses and that the Dow Chemical Company screens potential customers to determine how they intend to use it.

4.4 DISPOSAL

1,1,2-Trichloroethane has been disposed of by adsorption on a suitable sorbent such as vermiculite, dry sand, or earth and placement in a secure landfill (NLM 1988). This method is not recommended, however (NLM 1988), although no alternative method was discussed in the available literature. The method of disposal recommended for most chlorinated solvents is incineration.

4.5 ADEQUACY OF THE DATABASE

4.5.1 Data Needs

Data on current production and use of 1,1,2-trichloroethane are completely inadequate. Information is especially needed on the commercial uses of 1,1,2-trichloroethane and what types of consumer products, if any, contain this chemical. This information is essential for estimating exposure to 1,1,2-trichloroethane and for determining which groups in the population are occupationally or generally exposed. According to the Emergency Planning and Community Right to Know Act of 1986 (EPCRTKA), (§313), (Pub. L. 99-499, Title III, §313), industries are required to submit release information to the EPA. The Toxic Release Inventory (TRI), which contains release information for 1987, became available in May of 1989. This database will be updated yearly and should provide a more reliable estimate of industrial production and emission.

5. POTENTIAL FOR HUMAN EXPOSURE

5.1 OVERVIEW

1,1,2-Trichloroethane is predominantly a man-made chemical whose presence in the environment results from anthropogenic activity. This chemical has also been identified as an intermediate in the biodegradation of 1,1,2,2-tetrachloroethane, another man-made chemical. It is made commercially by the chlorination of ethylene with chlorine or by the oxychlorination of ethylene with HCl and oxygen. It is primarily used as a captive intermediate in the manufacture of 1,1-dichloroethene (vinylidene chloride), but may also be used as a solvent, especially in chlorinated rubber manufacture. Production and use information are proprietary, however effluent monitoring data indicate that high levels (>100 ppb) of discharge are associated with laundries, and the organic chemicals and mechanical products industries (Table 5-l). The maximum levels in these waste-waters were 109-250 ppb. Gaseous releases include vent gas and fugitive emissions from the production and use of 1,1,2-trichloroethane as well as volatilization from wastewater and municipal treatment plants. Releases to soil are expected to involve the landfilling of sludge and process residues. Thus far, 1,1,2-trichloroethane has been found at 45 of 1177 hazardous waste sites on the National Priorities List (NPL) in the United States (VIEW Database 1989). Based on the release pattern of other chlorinated ethanes and ethenes, it is expected that the release pattern for 1,1,2-trichloroethane is 70-90% to air, l0-30% to land, and a few percent to water. No use with significant consumer, and general population exposures has been identified.

If 1,1,2-trichloroethane is released into soil, it is expected to partially leach into the subsurface and groundwater (because it has a low soil adsorption coefficient), and to partially volatilize. In groundwater, it will be subject to anaerobic biodegradation, however no information concerning reaction rates is available. Biodegradation is expected to occur in sediment and landfills when anaerobic conditions are present. The mechanism for biodegradation is reductive dehalogenation, which leads to the formation of vinyl chloride, a human carcinogen (USDHHS 1985). From the limited data available, biodegradation under aerobic conditions, such as exists in surface soil, will be very slow, at best. In surface water, volatilization is the primary fate process (half-life 4.5 hr in a model river). Adsorption to sediment, bioconcentration in aquatic organisms, aerobic biodegradation, and hydrolysis are thought to be negligible by comparison. In the atmosphere, the dominant removal process is expected to be oxidation by photochemically-generated hydroxyl radicals, which proceeds by H-atom abstraction (estimated half-life 49 days). The radical so produced subsequently reacts with atmospheric oxygen and other atmospheric species. Removal from the atmosphere is also thought to occur from washout by precipitation; however, most of the 1,1,2-trichloroethane removed by this process is expected to reenter the atmosphere by volatilization. Because oxidation in the atmosphere is slow, considerable dispersion of

5. POTENTIAL FOR HUMAN EXPOSURE

TABLE 5-1. Sources of 1,1,2-Trichloroethane Effluents[a]

Industry	Frequency	Concentration (ppb)		
		Maximum	Medium	Low
Timber products	1	18.46	18.46	18.46
Organics and plastics	1	7.12	7.12	7.12
Inorganic chemicals	2	6.00	4.00	2.01
Plastics and synthetics	2	31.85	3.65	0.26
Auto and other laundries	1	108.99	108.99	108.99
Organic chemicals	1	203.77	203.77	203.77
Mechanical products	4	249.52	45.74	1.33
Transportation equipment	3	75.33	66.34	24.53
Synfuels	1	2.43	2.43	2.43
Publicly owned treatment works	4	15.22	1.20	0.42

[a]Discharges to water
Source: Shackelford et al. 1983

1,1,2-trichloroethane from source areas would be expected to occur. Thus, it is conceivable that 1,1,2-trichloroethane could be transported from other countries where it may be more widely used.

The general population may be exposed to low levels of 1,1,2-trichloroethane through inhalation of contaminated ambient air. Limited monitoring data suggest that roughly one-quarter to one-half of the urban population may be so exposed. Where 1,1,2-trichloroethane is found, levels appear to be about l0-50 ppt. Results from a nationwide monitoring study of groundwater supplies show that exposure to 1,1,2-trichloroethane from contaminated drinking water appears to be uncommon (Westrick et al. 1984). However, in a New Jersey survey, 6.7% of the wells contained detectable levels of 1,1,2-trichloroethane; the most polluted wells being associated with urban land use (Page 1981; Greenberg et al. 1982). It is difficult to assess occupational exposure because data on current production and use are unavailable. A National Occupational Exposure Survey (NOES) by the National Institute of Occupational Safety and Health (NIOSH) through May 1988, estimates that 1,036 employees are potentially exposed to 1,1,2-trichloroethane in the United States. Occupational exposure will be primarily via inhalation.

5.2 RELEASES TO THE ENVIRONMENT

5.2.1 Air

1,1,2-Trichloroethane is emitted in vent gas when produced by the oxychlorination of ethylene dichloride (Liepins et al. 1977). Environmental releases of 1,1,2-trichloroethane from l,l-dichloroethene manufacture are small; an EPA study found no 1,1,2-trichloroethane in process vent gas (Thomas et al. 1982). 1,1,2-Trichloroethane is formed in small quantities and may be released in vent gas or fugitive emissions during the production of other chlorinated hydrocarbons, for example, 1,2-dichloroethane and l,l,l-trichloroethane (Thomas et al. 1982). Fugitive emission from its use as a solvent and volatilization from wastewater constitute the major environmental release of 1,1,2-trichloroethane. An estimate of the total release of 1,1,2-trichloroethane was made for 1979 by comparing ambient levels of l,l,l-trichloroethane and 1,1,2-trichloroethane in urban air and releases of l,l,l-trichloroethane (Thomas et al. 1982). The annual amount of 1,1,2-trichloroethane released annually was calculated to be 10,000-20,000 million tons.

A correlation of data from the EPA Air Toxics Emission Inventory with industrial source categories (SIC codes), shows that volatile emissions of 1,1,2-trichloroethane are associated with plastic materials and resins, industrial organic chemicals, petroleum refining, gaskets-packing and sealing devices, plating and polishing, residential lighting fixtures, radio and TV communication equipment, electronic components, motor vehicles parts and accessories, engineering and scientific instruments, photographic

equipment and supplies (SIC Codes 2821, 2869, 2911, 3293, 3471, 3645, 3662, 3679, 3714, 3811, 3861) (EPA 1987a).

1,1,2-Trichloroethane was found at hazardous waste sites that are included in the National Priorities List (NPL). Volatile organic compound (VOC) emissions are observed at solid waste landfills (these emissions are 2.6-times greater in a wet climate than a dry one (Vogt et al. 1987)). Therefore low levels of 1,1,2-trichloroethane may be expected in landfill gases from NPL sites.

5.2.2 Water

Wastewater streams from the production of 1,1,2-trichloroethane by liquid-phase chlorination of ethylene dichloride and the oxychlorination of ethylene dichloride with HCl contain 1,1,2-trichloroethane (Liepins et al. 1977). Information on industries that discharge 1,1,2-trichloroethane, the frequency of discharge, and concentration levels can best be obtained from the results of a comprehensive wastewater survey conducted by the Effluent Guidelines Division of the EPA shown in Table 5-l. Over 4000 samples of wastewater from a broad range of industrial facilities and publicly-owned treatment works were analyzed in this survey. While the percentage of industries in a particular category containing 1,1,2-trichloroethane or the volume of wastewater generated by them was not indicated, the data suggest that significant amounts of 1,1,2-trichloroethane are released into waterways nationwide (see Table 5-l). Between 1980 and 1988, 707 samples of wastewater in EPA's STORET database were analyzed for 1,1,2-trichloroethane (STORET 1988). Ten percent of the samples contained 10 parts per billion (ppb) or higher concentrations of 1,1,2-trichloroethane and the maximum level obtained was 360 ppb. Unfortunately, the detection limit is apparently recorded when no chemical is detected, so it is impossible to say whether the 90 percentile figure represents positive samples or merely higher detection limits. EPA investigated priority pollutants in 40 geographically distributed publicly-owned treatment works (POTWs) representing a variety of municipal treatment technologies, size ranges, and industrial flow conditions. In this study, 1,1,2-trichloroethane was detected in 7% of influent samples, 3% of effluent samples, and 4% of raw sludge samples at maximum concentrations of 135, 6, and 2100 ppb, respectively (EPA 1982c).

1,1,2-Trichloroethane was found at concentrations of 2.1, 26, and 180 ppb in three outfalls from the Dow Chemical of Canada plant into the St. Clair River for a net loading of 3.5 kg/day (King and Sherbin 1986). Puddles containing chlorinated hydrocarbons had been discovered on the bottom of the St. Clair River, which received these effluents (King and Sherbin 1986; Kaiser and Comba 1986). These chemicals are thought to be products or byproducts of chlorinated hydrocarbons manufactured at this site. Waste from this operation is now being incinerated but was historically landfilled. Landfill leachate from the landfill is treated with carbon and then discharged into a ditch leading to the St. Clair River.

The concentration of 1,1,2-trichloroethane before and after treatment was 1,300 and 1,800 ppb. However the carbon filter was reportedly spent at the time of the survey.

1,1,2-Trichloroethane was detected in two samples at 2-3 ppb from Eugene, OR in the National Urban Runoff Program, in which 86 samples of runoff from 19 cities throughout the U.S. were analyzed (Cole et al. 1984). Runoff water from NPL hazardous waste sites containing 1,1,2-trichloroethane might be contaminated with this pollutant. No monitoring studies of runoff water from wastes sites was found in the available literature.

5.2.3 Soil

No information on the release of 1,1,2-trichloroethane to soil was found in the available literature. It is anticipated that process residues and sludge containing this chemical may be landfilled (Jackson et al. 1984). In an experiment designed to simulate the anaerobic conditions for biodegradation in landfills, 1,1,2-trichloroethane was found to be a biodegradation product of 1,1,2,2-tetrachloroethane (Hallen et al. 1986). Therefore 1,1,2.-trichloroethane may be produced in landfills or other anaerobic environments (e.g. groundwater) that have been contaminated with 1,1,2,2-tetrachloroethane.

5.3 ENVIRONMENTAL FATE

5.3.1 Transport and Partitioning

Based on a measured Henry's Law Constant of 9.1×10^{-4} atm/m^3-mol (Ashworth et al. 1988), the volatilization half-life of 1,1,2-trichloroethane in a model river 1 m deep flowing 1 m/set with a wind of 3 m/set is estimated to be 4.5 hr, with resistance in the liquid phase primarily controlling volatilization (Thomas 1982). The half-life in a lake or pond would be much longer. The half-life of 1,1,2-trichloroethane in the lower Rhine river was 1.9 days (Zoeteman et al. 1980). This determination was based on monitoring data and river flow data. This half-life was ascribed to volatilization. In wastewater treatment plants that receive refractory volatile compounds such as 1,1,2-trichloroethane from industrial discharges or other sources, stripping will be an important mechanism for transferring the chemical from the water into the air. In stripping, as opposed to ordinary volatilization, the liquid and gas phases are dispersed with the result that the interfacial surface area is much greater and liquid/gas mass transfer greatly enhanced. In 5 pilot scale treatment plants, 98 - >99% of 1,1,2-trichloroethane was removed by this process (EPA 1981). In view of its moderately high vapor pressure and low adsorptivity to soil, 1,1,2-trichloroethane is expected to volatilize rapidly from soil surfaces. In one experiment in which 1,1,2-trichloroethane was applied to a column of sandy soil with a very low organic carbon content, volatilization and leaching were equally important transport processes (Thomas et al. 1982).

The adsorption based on organic carbon, K_{oc}, of 1,1,2-trichloroethane on a sandy forest soil (low organic carbon content and cation exchange capacity, CEC), an agricultural soil, and a forest soil (pH lower than the agricultural soil) was 60.0, 63.7, and 108, respectively (Seip et al. 1986). In soil column experiments with these soils, the 1,1,2-trichloroethane moved through the sandy forest soil almost at the same rate as water, whereas the retardation was progressively greater in the agricultural soil and greatest in forest soil; the respective retention coefficients (velocity of water through the soil divided by the velocity of pollutant through the soil) being 1.53, 4.52, and 8.11 (Seip et al. 1986). Therefore 1,1,2-trichloroethane would not adsorb appreciably to soil, sediment, and suspended solids in the water column and would be expected to readily leach into the subsurface soil and groundwater. A second investigator obtained a Koc of about 70 and a retardation factor of <1.5 using a sandy soil of lower organic carbon content than that used in the first study (Wilson et al. 1981).

The bioconcentration factors for 1,1,2-trichloroethane reported in the literature are <10 (Kawasaki 1980) and 17 (Isnard and Lambert 1988). Therefore it would not be expected to bioconcentrate in fish to any great extent.

5.3.2 Transformation and Degradation

5.3.2.1 Air

In the atmosphere, 1,1,2-trichloroethane will be degraded by reaction with photochemically-produced hydroxyl radicals. The reaction proceeds by H-atom abstraction to yield water and the corresponding $C_2H_2Cl_3$ radical. The rate of this reaction is 3.28×10^{-13} cc/molecules-set which would give rise to a half-life of 49 days, assuming an average hydroxyl radical concentration of 5×10^5 radicals/cc (Jeong et al. 1984).

5.3.2.2 Water

1,1,2-Trichloroethane undergoes both a pH-independent and a basecatalyzed hyrolysis at environmental pH's. The neutral hydrolysis process is a substitution reaction leading to the formation of an alcohol, while the base-catalyzed reaction is an elimination reaction giving rise to l,ldichloroethene and HCl (Mabey et al. 1983; Vogel et al. 1987). In the case of 1,1,2-trichloroethane, the base-catalyzed rate is 5.9×10^{-3} l/mol-set at 25°C and is dominant above pH 5.4; the neutral rate is only 9x10-8 sec^{-1} at 80°C (Mabey et al. 1983). The half-life would be 37 years at pH 7 and 135 days. at pH 9. This is consistent with observations that no significant decrease in concentration occurs in 8 days in sterilized water (Jensen and Rosenberg 1975). No significant degradation was obtained in seawater, (pH 7.4-7.7) in 14 days at a temperature of ll-12°C (Jensen and Rosenberg 1975).

1,1,2-Trichloroethane showed no biodegradation in both a 24-day modified shake flask test and a river die-away test (Mudder and Musterman 1982). In two other biodegradabation screening tests, one investigator reported no degradation and the other slow degradation after a long acclimation period (Kawasaki 1980; Tabak et al. 1981). However the unknot extent to which volatilization contributed to losses in the second study makes the results suspect.

Under anaerobic conditions, 1,1,2-trichloroethane is reported to undergo dehalogenation. In order to establish whether this is a biologically mediated reaction and not simply an abiotic reaction catalyzed by free iron or iron porphyrin at low redox potential, Dow Chemical conducted 28-day studies in sterile solutions (Klecka and Gonsior 1983). They found that ppm concentrations of 1,1,2-trichloroethane did not undergo nonenzymatic dehalogenation in a sterile, anaerobic solution at pH 7 or when a sulfide redox buffer or hematin was added (Klecka and Gonsior 1983).

5.3.2.3 Soil

The only study located regarding the degradation of 1,1,2-trichloroethane in soil involved subsurface samples taken from the margin of a floodplain near Lula, Oklahoma (Wilson et al. 1983). These samples were obtained both above the water table of a shallow aquifer and in the unconsolidated material in the saturated zone. A portion of the soil *was* sterilized and slurries were made and test chemical added. Manipulations made with samples from the saturated zone were carried out under nitrogen. After 16 weeks of incubation, no degradation of 1,1,2-trichloroethan was observed in the samples from above or below the water table. These results are in conflict with other studies (Wilson et al. 1983). It has been suggested that the time frame for the experiment may have been insufficient for resident microorganisms to have become acclimated to the chemical (Newsom 1985).

In an attempt to simulate the anaerobic conditions for biodegradation in landfills, experiments were performed under anoxic conditions using inocula from anaerobic digester units of wastewater treatment facilities that were not acclimated to industrial solvents. After 1 week of incubation with 10 μg/L of 1,1,2-trichloroethane, 0.44 μg/g of vinyl chloride was formed, the highest level observed from any of the chlorinated ethanes or ethenes studied (Hallen et al. 1986). In further experiments when the concentration of inoculum was increased, 4.3 and 5.8 μg/g of vinyl chloride was formed after 1 and 2 weeks, respectively. The degradation reactions observed not only include reductive dehalogenation but the transformation of chlorinated ethanes into ethenes. It is interesting to note that autoclaved controls for a 1,1,2-trichloroethane anaerobic biodegradation experiment yielded l,l,-dichloroethene (Molton et al. 1987). The formation of l,ldichloroethene indicates that the conversion of 1,1,2-trichloroethane is nonbiological.

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

5.4.1 Air

Two air samples from rural Oklahoma and air samples from rural areas of the Pacific Northwest did not contain 1,1,2-trichloroethane (Brodzinsky and Singh 1982; Grimsrud and Rasmussen 1975). While both inland and nearshore rural sites near San Francisco averaged 14 parts per trillion (ppt) of 1,1,2-trichloroethane, 95% of inland sites and 46% of nearshore sites contained levels above the 6 ppt detection limit (Singh et al. 1977). In 930 urban/suburban sites in the U.S. the 25th, 50th, 75th percentile and maximum concentration of 1,1,2-trichloroethane was 0, 9.1, 22, and 11,000 ppt, respectively (Brodzinsky and Singh 1982). Other studies that include 13 major U.S. cities, report average air concentrations of 1,1,2-trichloroethane ranging from 6-41 ppt (Singh et al. 1981; Singh et al. 1982; Harkov et al. 1983; Lioy et al. 1983). In the study by Harkov et al., (1983) air concentrations in Camden, Elizabeth, and Newark, NJ were monitored during the summer of 1981. Of the 111 samples measured, 27% contained a detectable quantity of the pollutant, with a detection limit of 5 PPt. The following winter, 41% of the samples from these cities contained 1,1,2-trichloroethane. The geometric mean concentrations ranged from 20-50 ppt for the winter measurements. This was significantly higher than the 10 ppt value obtained the previous summer (Harkov et al. 1987). The median concentration of 1,1,2-trichloroethane in 97 samples obtained from source-related areas throughout the U.S. was 45 ppt. Of these samples, 25% exceeded 210 ppt and a maximum concentration was 2,300 ppt was measured in Dominguez, CA (Brodzinsky and Singh 1982). The data compiled by Brodzinsky and Singh (1982) has been reviewed and most of it is of good quality. More data have now been added to this National Ambient Volatile Organic Compounds Database bringing the number of monitoring data points to 886 (Shah and Heyerdahl 1988). According to this database, the median concentration of 1,1,2-trichloroethane in rural, suburban, and urban areas was 0 ppt; at source-dominated sites the median 1,1,2-trichloroethane concentration was 2 PPt. The limited monitoring data suggest that roughly one-quarter to one-half of the urban population may be exposed to the compound in air. Where 1,1,2-trichloroethane is found, most levels range from l0-50 ppt.

The only data on levels of 1,1,2-trichloroethane measured in indoor air were contained in a study of eight homes in Knoxville, TN obtained during the winter (Gupta et al. 1984). Eleven of sixteen samples contained 1,1,2-trichloroethane with a mean [SD] concentration of 14.1 [7.8] $\mu g/m^3$ (2.5 [l.4] ppb), however samples taken outside the homes did not contain detectable levels of the chemical. Sources of the 1,1,2-trichloroethane inside the homes may be building materials or solvent-containing products.

Traces to 0.32 ppb of 1,1,2-trichloroethane in air samples were found in Iberville Parish, Louisianna, where many organic chemical and producer, user, and storage facilities are located along the Mississippi River (Pellizarri 1982).

5.4.2 Water

1,1,2-Trichloroethane was not detected in composite samples of the water supplies of Philadelphia, PA and Huntington, WV, both of which are derived from surface sources (Dreisch et al. 1980). The levels in finished water from a New Orleans, LA water supply ranged from 0.1 to 8.5 ppb (EPA 1980). In a l0-city EPA survey conducted in 1975, 1,1,2-trichloroethane was only detected in the water supply of Miami, FL, which obtains its water from a groundwater source (EPA 1975). The level of contamination was not determined. The maximum concentration of 1,1,2-trichloroethane detected in a survey of community and noncommunity water supplies from groundwater sources and private wells in Suffolk County, NY, was 13 ppb (Zaki et al. 1986). 1,1,2-Trichloroethane has been found in 10 private wells in Rhode Island, at a concentration range of 1.0 to 14.0 ppb (RIDH 1989). A survey of Denver, CO, drinking water conducted in late 1985 to early 1986, found no 1,1,2-trichloroethane in the samples tested (Rogers et al. 1987). In a U.S. Groundwater Supply survey, none of the 945 groundwater supply sources tested contained 1,1,2-trichloroethane at a quantitation limit of 0.5 ppb (Westrick et al. 1984). 1,1,2-Trichloroethane was found in 6 of the 1174 community wells and 19 of the 617 private wells in a Wisconsin survey conducted in the early 1980s (Krill and Sonzogni 1986). All wells contained less than the recommended health advisory level of 6.1 ppb. Representative samples of ground and surface water were analyzed from the state of New Jersey during 1977-1979 (Page 1981). These samples were collected from every county, from urban, suburban, and rural areas, and from areas of every land use common in the state. Seventy-two of the 1069 groundwater samples (6.7%) and 53 of the 603 surface water samples (8.7%) contained detectable levels of 1,1,2-trichloroethane with concentrations as high as 31.1 and 18.7 ppb being found for ground and surface water, respectively. Some of the most polluted wells were under urban land use areas (Page 1981, Greenberg et al. 1982). Ground water near landfill sites in Minnesota and Wisconsin contained up to 31 ppb of 1,1,2-trichloroethane (Sabel and Clark 1984).

Of 7 samples from two Ohio River tributaries, 3 were positive for 1,1,2-trichloroethane (0.6 ppb maximum). However, only 4% of the samples from the Ohio mainstream were positive and the compound was not found in 88 additional stations (Ohio River Valley Sanitation Commission 1980). One measurement of 1,1,2-trichloroethane in marine water was found, 153 ppt off the shore at Point Reyes, CA (Singh et al. 1977).

Between 1980 and 1988, 3255 samples of surface water in EPA's STORET database were analyzed for 1,1,2-trichloroethane (STORET 1988). Ten percent of the samples contained the chemical at 10 parts per billion (ppb) or higher. A maximum level of 18,000 ppb was reported in 1982. The maximum concentration of 1,1,2-trichloroethane reported for subsequent years ranged from 10 to 125 ppb. Of the 22,615 samples of groundkater in the database, 10% were above 3 ppb. The maximum concentration of 1,1,2-trichloroethane in a groundwater was 350,000 ppb, reported in 1985. For the other years, the

maximum concentration reported ranged from 18 to 1800 ppb. Unfortunately, the detection limit is apparently recorded in STORET when no chemical is detected, so it is impossible to say whether the 90 percentile figure represents positive samples or merely higher detection limits.

5.4.3 Soil

1,1,2-Trichloroethane was found in 25 of the 418 hazardous waste sites listed on the National Priorities List of highest priority sites for possible remedial action (Mitre 1987). Additionally, it was found in 3 sites in the Contract Laboratory Statistical Database at mean concentrations ranging from 12 to 636 ppb (Viar and Company 1987).

5.4.4 Other Media

1,1,2-Trichloroethane was detected in 9 of 22 commercial batches of technical grade l,l,l-trichloroethane supplied by eight different European manufacturers and dealers (Henschler et al. 1980). The concentration in these samples ranged from 300 to 3,015 ppm and the detection limit was 0.5 PPm. It was also found in some commercially available trichloroethylene in Japan (Tsuruta et al. 1983).

1,1,2-Trichloroethane was not detected in any of the 46 composite samples of human adipose tissue collected during FY82 as part of the National Human Adipose Tissue Survey (Stanley 1986). The composite specimens represented the nine U.S. census divisions stratified by three age groups (0-14, 15-44, 45 plus). Between July and December 1980, air and breath from nine New Jersey subjects were monitored in a pilot study to measure personal exposure to volatile organic substances for EPA's Total Exposure Assessment Methodology (TEAM) Study (Wallace et al. 1984). The personal air concentrations of 1,1,2-trichloroethane were below the detection limit in 151 of 161 of the samples, 7 contained trace levels of the chemical and the others ranged from 0.14 to 34.70 $\mu g/m^3$ (0.025 to 6.25 ppb), with a median of 0.35 $\mu g/m^3$ (0.063 ppb) (Wallace et al. 1984). Breath samples were negative in 44 of 49 samples and the others ranged from trace to 5.13 $\mu g/m^3$ (0.92 ppb), with a median of 0.2 $\mu g/m^3$ (0,036 ppb). No 1,1,2-trichloroethane was found in the subjects' drinking water at home.

5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

A National Occupational Exposure Survey (NOES) conducted by NIOSH from 1981 to 1983 estimates that 1036 workers, including 15 women, are potentially exposed to 1,1,2-trichloroethane in the United States (NIOSH 1988). The estimate is provisional, as all of the data for trade name products which may contain 1,1,2-trichloroethane have not been analyzed. The NOES survey was based on field surveys of 4,490 facilities and was designed as a nationwide survey based on a statistical sample of virtually all workplace environments in the United States where eight or more persons are employed in all SIC codes except mining and agriculture. In the earlier

NIOSH National Occupational Hazard Survey, the highest exposures occurred around blast furnaces, in steel rolling mills and in factories manufacturing technical instruments (Konietzko 1984).

Consistent with its tendency to partition into air, most exposures to 1,1,2-trichloroethane are from air. Limited monitoring data suggest that one-quarter to one-half of the urban population may be exposed *to* the compound in air. Where 1,1,2-trichloroethane is found, levels appear to be about l0-50 ppt, for an average daily intake of 1.1-5.5 μg/day. It appears that the general population is rarely exposed to 1,1,2-trichloroethane in drinking water.

5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURE

If people use products containing 1,1,2-trichloroethane as a solvent, they will be potentially exposed to high levels of this chemical. Moolenaar and Olson (1989), in a written communication as spokesmen for the Dow Chemical Company, however, stated that they are not aware of any consumer uses and that the Dow Chemical Company screens potential customers to determine how they intend to use the 1,1,2-trichloroethane they purchase. Therefore, the potential for exposure from use of consumer products is probably low.

While it appears that exposure to high levels of 1,1,2-trichloroethane is rare, there are a few data that indicate that a small number of people may be exposed to high levels of 1,1,2-trichloroethane from contaminated air or drinking water. In Lake Charles, LA, the median and maximum air concentrations of 1,1,2-trichloroethane were 4.8 and 7.4 ppb (Brodzinsky and Singh 1982). This indicates that half of the population of this community have a daily intake of 530 to 820 μg/g, compared with a median intake of 2.6 μg/g for all the urban/suburban areas of the United States that were monitored. Other cities where air concentrations greater than 0.1 ppb were sometimes observed were Elizabeth, NJ, Deer Park, TX, Freeport, TX, Geismar, LA, Edison, NJ, and Domingues, CA (Brodzinsky and Singh 1982). The data indicate that the air concentrations are variable, and only occasionally are high levels of 1,1,2-trichloroethane observed. From the available data, it is apparent that some wells in Suffolk County, NY, New Jersey, and near landfills in Minnesota and Wisconsin contain 1,1,2-trichloroethane concentrations as high as 13 to 31 ppb, corresponding to an average daily intake of 26 to 62 μg/g per day. The available data are insufficient to estimate the number of people that may be exposed to high levels of 1,1,2-trichloroethane.

5.7 ADEQUACY OF THE DATABASE

5.7.1 Data Needs

Physical and Chemical Properties. The physical and chemical properties of 1,1,2-trichloroethane have been adequately characterized (see Table 3.2).

Environmental Fate. Further investigation would resolve the discrepancies in the data for anaerobic degradation of 1,1,2-trichloroethane. Additional studies are needed to characterize the nature of the transformation and to clarify whether biotic, abiotic, or catalyzed abiotic reactions are involved. Will these reactions generally occur under environmental conditions? A determination of the half-life in representative groundwater and sediment-water systems would be useful. From the available evidence, biodegradation in aerobic systems appears unlikely, although additional studies, particularly in soil, are desireable and would clarify this point.

Exposure Levels in Environmental Media. The best estimates of exposure are based on monitoring data and these data add credence to emission and exposure estimates based on production and use. In the case of 1,1,2-trichloroethane, monitoring data are fragmentary and not very recent; most of the data are from the early 1980s or earlier. Information on production and use, particularly that with the largest probability for exposure, is not available. While 1,1,2-trichloroethane may be contained in some consumer products, the Dow Chemical Company is not aware of any consumer uses (Moolenaar and Olson 1989).

Exposure Levels in Humans. Estimates of general population and occupational exposure require current monitoring data or current data on production and use. This information is not available. The use pattern of 1,1,2-trichloroethane may have changed since the NOES. If this is the case, the results of the NOES could be reanalyzed in order to reflect current occupational exposures.

Exposure Registries. Other than the NIOSH survey, no exposure registries for 1,1,2-trichloroethane were located. The development of a registry of exposed persons would provide a useful reference tool in assessing exposure levels and frequency. In addition, a registry would allow an assessment of the variations in exposure concentrations by, for example, geography, season, regulatory actions, presence of hazardous waste landfills, or manufacturing or use facility. These assessments, in turn, would provide a better understanding of the needs for some types of research or data acquisition based on the current exposure concentrations. Additionally, such a database of exposures would be useful for linking exposure to 1,1,2-trichloroethane with specific toxic effects or diseases.

5.7.2 On-going Studies

No information was found which would indicate that there are studies in progress that relate to the environmental fate of 1,1,2-trichloroethane. As part of the Third National Health and Nutrition Evaluation Survey (NHANES III), the Environmental Health Laboratory Sciences Division of the Center for Environmental Health and Injury Control, Centers for Disease Control, will be analyzing human blood samples for 1,1,2-trichloroethane and other

volatile organic compounds. These data will give an indication of the frequency of occurrence and background levels of these compounds in the general population. NIOSH is continuing to revise its estimates of occupational exposures in its National Occupational Exposure Survey (NOES) through the inclusion of trade name compounds. No other on-going studies regarding general or occupational exposure to 1,1,2-trichloroethane were located. According to the Emergency Planning and Community Right to Know Act of 1986 (EPCRTKA), (§313), (Pub. L. 99-499, Title III, §313), industries are required to submit release information to the EPA. The Toxic Release Inventory (TRI), which contains release information for 1987, became available in May of 1989. This database will be updated yearly and should provide a more reliable estimate of industrial production and emission, which will be useful for determining potential human exposure.

6. ANALYTICAL METHODS

6.1 BIOLOGICAL MATERIALS

The analytical methods for the determination of 1,1,2-trichloroethane in biological matrices are given in Table 6-1. Very few studies exist in the literature that report the analyses of this compound in biological matrices. The discussion about the methods that may be most sensitive for the determination of 1,1,2-trichloroethane levels in environmental samples and the advantages and disadvantages of the commonly used methods as given for environmental samples are thought to be applicable for biological samples because identical quantification methods are used for both kinds of samples. Most biological samples, however, pose unique problems during quantification. For example, the binding of the analytes to protein in samples containing high protein (e.g., whole blood) may result in reduced recovery (Cramer et al. 1988). Both blood and urine are very susceptible to foaming, especially at-high temperatures used during purging (Cramer et al. 1988; Michael et al. 1980). Poor and variable recovery has also been observed for tissue samples with high lipid content (Michael et al. 1980).

6.2 ENVIRONMENTAL SAMPLES

The common methods used for the determination of 1,1,2-trichloroethane in environmental samples are given in Table 6-2. The two common methods that are used for the preconcentration of 1,1,2-trichloroethane for the determination of its levels in air are adsorption on a sorbent column or collection in a cryogenically-cooled trap. The disadvantage with the cryogenic cooling is that the method is cumbersome and condensation of moisture in the air may block the passage of further air flow through the trap. The disadvantages with the sorption tubes are that the sorption and desorption efficiencies may not be 100% and that the background impurities in the sorbent tubes may limit detection in samples containing low concentrations (Cox 1983).

The most common method for the determination of 1,1,2-trichloroethane levels in water, sediment, soil, and aquatic species is the purging of the vapor from the sample or its suspension in water with an inert gas and trapping the desorbed vapors in a sorbent trap. Subsequent thermal desorption is used for the quantification of its concentration.

The two quantification methods that provide the lowest detection limits are halide-specific detection (e.g., Hall electrolytic conductivity detector) and mass spectrometry. Since the compound has three chlorine atoms, electron capture detection is also very sensitive for this compound. The advantages of halide-specific detectors are that they are not only very sensitive but are also specific for halide compounds. The mass spectrometer, on the other hand, provides an additional confirmation of the presence of a compound through the ionization patterns, and is desirable

TABLE 6-1. Analytical Methods for 1,1,2-Trichloroethane in Biological Samples[a]

Sample Matrix	Sample Preparation	Analytical Method	Detection Limit	Accuracy	Reference
Exhaled air	Collected in Tedlar bag, adsorbed on Tenax and thermally desorbed	Cryofocussing HRGC-MS	NG	NG	Barkley et al. 1980
Blood and urine	Purge at 50°C, trap in Tenax, thermal desorption	Cryofocussing HRGC-MS	NG	NG	Barkley et al. 1980
Blood	Purge and trap in Tenax, thermally desorb	GC-MS	NG	NG	Cramer et al. 1988
Urine	Equilibriate in sealed vial at 37°C and headspace gas analyzed	HRGC-MS	NG	NG	Ghittori et al. 1987
Human milk	Purge at 70°C, trap in Tenax, desorb thermally	Cryofocussing HRGC-MS	NG	NG	Pellizzari et al. 1982 Michael et al. 1980

[a]Although the analytical methods given were used for 1,1,1-trichloroethane, these methods should be applicable to 1,1,2-trichloroethane.

NG = Not given; GC = gas chromatography; HRGC = high resolution gas chromatography; MS = mass spectrometry

TABLE 6-2. Analytical Methods for 1,1,2-Trichloroethane in Environmental Samples

Sample Matrix	Sample Preparation	Analytical Method	Detection Limit	Accuracy	Reference
Ambient air	Direct injection.	Subambient air MG-MS	<5 ppt	NG	Grimsrud and Rasmussen 1975
	Adsorption on Tenax, thermal desorption into a stainless steel cylinder.	Subambient HRGC-MS	0.01-0.1 ppb	NG	Harkov et al. 1985, Kebbekus and Bozzelli 1982
	Sample collected in a cryogenically cooled trap.	GC-ECD	<0.01 ppb	85-115%	Singh et al. 1982
Occupational air	Adsorption on charcoal, desorption by CS_2.	GC-FID (NIOSH Methods P & CAM 127 and 5134)	0.05 mg/sample	92.3%	NIOSH 1977a,b
Landfill air	Adsorption on Tenax, thermal desorption into a stainless steel cylinder.	Cryofocussing GC-MC	0.1 ppb[a]	NG	LaRegina et al. 1986
Drinking, ground and surface water	Vacuum distillation with cryogenic trapping.	HRGC-ECD	0.2 µg/L	54%	Comba and Kaiser 1983
Finished water and raw source water	Purge at ambient temperature, trap in Tenax/silica/charcoal and desorb thermally.	GC-HECD (EPA Method 502.1)	0.007 µg/L	95% at 0.4 µg/L	EPA 1986a
	Purge at ambient temperature, trap in Tenax/silica charcoal,	subambient programmable GC-MS (EPA Method 524.1)	NG desorb thermally.	NG	EPA 1986a
	Purge at ambient temperature, trap in Tenax/silica charcoal, thermally desorb.	Cryofocussing HRGC-MS (wide or narrow bore) (EPA Method 524.2)	0.1 µg/L (wide bore) 0.08 µg/L (narrow bore)	104% (wide bore) at 0.5-10.0 µg/L 102% (narrow bore) at 0.5 µg/L	EPA 1986a
Water/wastewater	Purge at ambient temperature, trap in Tenax/silica charcoal, thermally desorb.	GC-HECD (EPA Method 601)	0.02 µg/L	91% at 0.45-50.0	EPA 1982a

TABLE 6-2 (continued)

Sample Matrix	Sample Preparation	Analytical Method	Detection Limit	Accuracy	Reference
Water/wastewater	Purge at ambient temperature, trap in Tenax/silica, thermally desorb.	GC-MS (EPA Method 624)	5.0 µg/L	101-104%	EPA 1982a
Groundwater/ leachate	Purge at ambient temperature, trap in Tenax/silica, desorb thermally.	GC-MS (EPA-CLP Method)	5 µg/L	NG	EPA 1987a
	Purge at ambient temperature, trap in Tenax/silica/charcoal, desorb thermally.	GC-HECD (EPA Methods 5030 and 8010)	0.2 µg/L	0.86c + 0.30 (where c is the concentration	EPA 1982b, 1986b
Sediment	Closed-loop purging and steam distillation, trap in Porapak N, solvent desorption.	GC-MS	1 µg/L	77-91%	Amin and Narang 1985
Sediment/fish	Vacuum distillation and cryogenic condensation.	HRGC-MS	NG	98% (sediment) 66% (fish)	Hiatt 1981, 1983
Soil/sediment	Purge suspension in water at 50°C, trap in Tenax/silica, desorb thermally.	GC-MS (EPA-CLP Method)	5 µg/L	NG	EPA 1987a
Soil, sludge, liquid and solid	Sample dispersed in a glycol, purge at ambient temperature, trap in Tenax/silica, desorb thermally.	GC-HECD (EPA Method 5030 and 8010)	0.2 µg/kg (soil) 10 µg/kg (liquid waste) 25 µg/kg (sludge and solid waste)	0.86c + 0.30	EPA 1982b, 1986b

[a]Based on a detection limit equivalent to twice the laboratory and field blank samples.

GC = Gas chromatography; MS = mass spectrometry; NG = not given; HRGC = high resolution gas chromatography; FID = flame ionization detector; ECD = electron capture detector; HECD = Hall electrolytic conductivity detector

when a variety of compounds must be quantified. The inability of halide-specific detectors to detect and quantify non-halogen compounds can be greatly overcome by using other detectors (e.g., photoionization detector) in series (Lopez-Avila et al, 1987; Driscoll et al. 1987). High-resolution gas chromatography with capillary columns is a better method for volatile compounds than are packed columns because they provide better resolution of closely eluting compounds and increase the sensitivity of detection. In addition, purge and whole-column cryotrapping eliminates the need for the conventional purge-and-trap unit and reduces the time of analysis (Pankow and Rosen 1988). The plugging of the trap by the condensation of moisture during cryotrapping may be avoided by the use of a very wide-bore capillary column, although the chromatographic resolution of such a column is inferior to narrow-bore capillary columns (Pankow and Rosen 1988; Mosesman et al. 1987). Regardless of the analytical method used for biological and environmental samples, precautions should be taken during sampling, preservation, and storage of samples to prevent loss from volatilization.

6.3 Adequacy of the Database

6.3.1 Data Needs

Methods for Determining Parent Compounds and Metabolites in Biological Materials. The analytical methods for determining levels of volatile chlorinated compounds in biological media are general ones, applicable to the entire class of chemicals. The publications that describe these methods do not report either the recovery or the detection limit of 1,1,2-trichloroethane in different biological matrices. The study of the levels of the parent compound in human blood, urine or other biological matrices can be useful in deriving a correlation between the level of this compound found in the environment and those found in human tissue or body fluid. Such correlation studies are unavailable for this compound, although the parent compound has been detected in human breath and urine (see Subsection 2.4).

No metabolite of 1,1,2-trichloroethane from human exposure to this compound has yet been identified (see Subsection 2.6.3). The changes in metabolite concentrations with time in human blood, urine, or other appropriate biological medium may be useful in estimating its rate of metabolism in humans. In some instances, a metabolite may be useful in correlating the exposed doses to the human body burden. Such studies on the levels of metabolites in human biological matrices are not available for this compound, although metabolic products of this compound from animal and in vitro studies have been identified (see Subsection 2.6.3) and analytical methods for their quantification are available.

Methods for Biomarkers of Exposure. No studies were located that identified biomarkers specific for 1,1,2-trichloroethane-induced disease states (see Subsection 2.9.2). If a biomarker for this compound in a human biological tissue or fluid were available and a correlation were found to

exist between the level of biomarker and a certain health effect, it could be used as an indication of a health effect caused by the exposure to this chemical.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. As shown in Table 6-2, methods are available for the analysis of 1,1,2-trichloroethane in environmental samples. The levels of this compound in different environmental media can be used to indicate whether there could be human exposure to this compound through the inhalation of air and ingestion of drinking water and foods containing 1,1,2-trichloroethane. If a correlation with human tissue or body fluid levels were available, the intake levels from different environmental sources can be used to estimate the body burden of the chemical in humans.

Although the products of biotic and abiotic processes of this compound in the environment are adequately known, no systematic study is available that measured the concentrations of its reaction products in the environment. In instances where the product(s) of an environmental reaction is more toxic than the parent compound, it is important that the level of the reaction products in the environment be known. It is known that 1,1,2- trichloroethane under anaerobic conditions (e.g. in anaerobic soils leading to contamination to groundwater) may dehydrochlorinate to vinyl chloride (see Section 5.3), a compound more toxic than the parent compound. The analytical methods for the determination of the levels of these and other environmental degradation products of 1,1,2-trichloroethane are available.

6.3.2 Ongoing Studies

The Environmental Health Laboratory Sciences Division of the Center for Environmental Health and Injury Control, Centers for Disease Control, is developing methods for the analysis of 1,1,2-trichloroethane and other volatile organic compounds in blood. These methods use purge and trap methodology and magnetic mass spectrometry which gives detection limits in the low parts per trillion range.

7. REGULATIONS AND ADVISORIES

International, national, and state regulations and guidelines pertinent to human exposure to 1,1,2-trichloroethane are summarized in Table 7-1.

1,1,2-Trichloroethane is regulated by the Clean Water Effluent Guidelines for the following industrial point sources: electroplating, organic chemicals, steam electric, asbestos, timber products processing, metal finishing, paving and roofing, paint formulating, ink formulating, gum and wood, carbon black, and electrical and electronic components (EPA 1988b).

7. REGULATIONS AND ADVISORIES

TABLE 7-1. Regulations and Guidelines Applicable to 1,1,2-Trichloroethane

Agency	Description	Value	Reference
	International		
IARC	Cancer Classification	3[a]	IARC 1987
	National		
Regulations			
a. Air:			
OSHA	Permissible Exposure Limit	10 ppm	OSHA 1989 29 CFR 1910.1000
b. Water:			
EPA OWRS	Ambient Water Quality Criterion: For consumption of water and organisms For consumption of organisms only	 0.6 µg/L 41.8 µg/L	45 FR 79318 EPA 1980 (11/28/80)
c. Nonspecific media:			
EPA OERR	Reportable Quantity	100 lbs	52 FR 8140 40 CFR 117, 302 (03/16/87)
Guidelines			
a. Air:			
ACGIH	TWA for 8-hr workday Occupational Exposure	10 ppm	ACGIH 1988
b. Water:			
EPA	Required Monitoring in Community Water Systems		52 FR 25715 (07/08/87) 40 CFR 141, 142
EPA ODW	One Day Health Advisory Ten Day Health Advisory Long Term Health Advisory (10 kg child) Long Term Health Advisory (70 kg adult) Lifetime Health Advisory	600 µg/L 400 µg/L 400 µg/L 1000 µg/L 3 µg/L	EPA 1987 EPA 1987 EPA 1987 EPA 1987 EPA 1987
c. Nonspecific media:			
EPA	RfD for chronic oral exposure	0.004 mg/kg/day	EPA 1988a
EPA	q1* for oral exposure q1* for inhalation exposure	0.057/mg/kg/day 0.057/mg/kg/day	EPA 1988a EPA 1988a verified 7/23/86
EPA	Cancer Classification	c[b]	EPA 1988a
EPA RCRA	Listed		52 FR 25942 (07/09/87) 40 CFR 260
EPA	Listed as a Hazardous Substance		51 FR 6541 (02/25/86) 40 CFR 261

7. REGULATIONS AND ADVISORIES

TABLE 7-1 (continued)

Agency	Description	Value	Reference
	State		
State Agencies			
a. Air:	Acceptable ambient air concentrations		
Kentucky		4.5 mg/m^3 (8-hour avg)	401 KAR 63:022
b. Water:	Drinking Water quality guidelines		FSTRAC 1988
Arizona		1 µg/L	
California		100 µg/L	
Minnesota		6 µg/L	
New Mexico		10 µg/L	

[a]Group 3 - Not classifiable as to its carcinogenicity in humans
[b]Group C - Possible human carcinogen

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9. GLOSSARY

Acute Exposure -- Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

Adsorption Coefficient (Koc) -- The ratio of the amount of a chemical adsorbed per unit weight of organic carbon in the soil or sediment to the concentration of the chemical in solution at equilibrium.

Adsorption Ratio (Kd) -- The amount of a chemical adsorbed by a sediment or soil (i.e., the solid phase) divided by the amount of chemical in the solution phase, which is in equilibrium with the solid phase, at a fixed solid/solution ratio. It is generally expressed in micrograms of chemical sorbed per gram of soil or sediment.

Bioconcentration Factor (BCF) -- The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same period.

Cancer Effect Level (CEL) -- The lowest dose of chemical in a study, or group of studies, that produces significant increases in the incidence of cancer (or tumors) between the exposed population and its appropriate control.

Carcinogen -- A chemical capable of inducing cancer.

Ceiling value (DL) -- A concentration of a substance that should not be exceeded, even instantaneously.

Chronic Exposure -- Exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Developmental Toxicity -- The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

Embryotoxicity and Fetotoxicity -- Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the insult occurred. The terms, as used here, include malformations and variations, altered growth, and in utero death.

EPA Health Advisory -- An estimate of acceptable drinking water levels for a chemical substance based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials,

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Immediately Dangerous to Life or Health (IDLH) -- The maximum environmental concentration of a contaminant from which one could escape within 30 min without any escape-impairing symptoms or irreversible health effects.

Intermediate Exposure -- Exposure to a chemical for a duration of 15-364 days as specified in the Toxicological Profiles.

Immunologic Toxicity -- The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

In vitro -- Isolated from the living organism and artificially maintained, as in a test tube.

In vivo -- Occurring within the living organism.

Lethal Concentration($_{LO}$) (LC_{LO}) -- The lowest concentration of a chemical in air which has been reported to have caused death in humans or animals.

Lethal Concentration($_{50}$) (LC_{50}) -- A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

Lethal Dose($_{LO}$) (LD_{LD}) -- The lowest dose of a chemical introduced by a route other than inhalation that is expected to have caused death in humans or animals.

Lethal Dose($_{50}$) (LD_{50}) -- The dose of a chemical which has been calculated to cause death in 50% of a defined experimental animal population.

Lethal Time($_{50}$) (LT_{50}) -- A calculated period of time within which a specific concentration of a chemical is expected to cause death in 50% of a defined experimental animal population.

Lowest-Observed-Adverse-Effect Level (LOAEL) -- The lowest dose of chemical in a study, or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Malformations -- Permanent structural changes that may adversely affect survival, development, or function.

Minimal Risk Level -- An estimate of daily human exposure to a chemical that is likely to be without an appreciable risk of deleterious effects (noncancerous) over a specified duration of exposure.

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Mutagen -- A substance that causes mutations. A mutation is a change in the genetic material in a body cell, Mutations can lead to birth defects, miscarriages, or cancer.

Neurotoxicity -- The occurrence of adverse effects on the nervous system following exposure to chemical.

No-Observed-Adverse-Effect Level (NOAEL) -- The dose of chemical at which there were no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

Octanol-Water Partition Coefficient (Kow) -- The equilibrium ratio of the concentrations of a chemical in n-octanol and water, in dilute solution.

Permissible Exposure Limit (PEL) -- An allowable exposure level in workplace air averaged over an 8-hour shift.

q_1^* -- The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The q_1^* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually μg/L for water, mg/kg/day for food, and $\mu g/m^3$ for air).

Reference Dose (RfD) -- An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the NOAEL (from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

Reportable Quantity (RQ) -- The quantity of a hazardous substance that is considered reportable under CERCLA. Reportable quantities are (1) 1 lb or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Sect. 311 of the Clean Water Act. Quantities are measured over a 24-hour period.

Reproductive Toxicity -- The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

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Short-Term Exposure Limit (STEL) -- The maximum concentration to which workers can be exposed for up to 15 min continually. No more than four excursions are allowed per day, and there must be at least 60 min between exposure periods. The daily TLV-TWA may not be exceeded.

Target Organ Toxicity -- This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

Teratogen -- A chemical that causes structural defects that affect the development of an organism.

Threshold Limit Value (TLV) -- A concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a TWA, as a STEL, or as a CL.

Time-weighted Average (TWA) -- An allowable exposure concentration averaged over a normal 8-hour workday or 40-hour workweek.

Toxic Dose (TD50) -- A calculated dose of a chemical, introduced by a route other than inhalation, which is expected to cause a specific toxic effect in 50% of a defined experimental animal population.

Uncertainty Factor (UF) -- A factor used in operationally deriving the RfD from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of human, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10.

APPENDIX

PEER REVIEW

A peer review panel was assembled for 1,1,2-trichloroethane. The Panel consisted of the following members: Dr. James V. Bruckner, Associate Professor and Director of Toxicology, University of Georgia College of Pharmacy; Dr. Richard J. Bull, Associate Professor of Pharmacology/ Toxicology, University of Washington; Dr. Mildred Christian, Argus Research Laboratories; and Dr. Curtis Klaasen, University of Kansas. These experts collectively have knowledge of 1,1,2-Trichloroethane's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in the Superfund Amendments and Reauthorization Act of 1986, Section 110.

A joint panel of scientists from ATSDR and EPA has reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply their approval of the profile's final content. The responsibility of the content of this profile lies with the Agency for Toxic Substances and Disease Registry.